Recommender Systems for Biomedical and Health informatics

Presented by:
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Outline

- Can we improve medicine?
- What does this have to do with recsys?
- Medical decision support systems
- ML medical decision systems

Medicine: what can be improved?

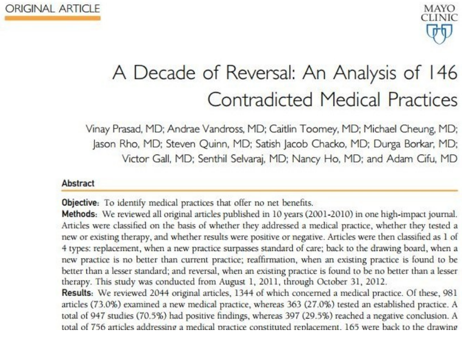
Medical decisions require knowledge & data

- Doctors have partial information
  - Of the patient's history
  - Of the patient's symptoms
  - Of medical knowledge
    - Different demographics
    - Latest research findings
    - Not easy to remember all past information
- They also might have cognitive biases
  - They decide mostly based on past experience, but this experience is very limited
- Incentives of medical industry also play a role

Experts disagree

- Experts disagree among themselves.
  - E.g. oncology experts disagree on the value of colon screening
- Things treated as facts for years end up being wrong.
  - E.g. giving aspirin to reduce fever has been proved to be dangerous
- Psychiatric disorder diagnosis even lower agreement

  (Cohen’s Kappa of 0.2 or 0.3 in most cases)



ORIGINAL ARTICLE

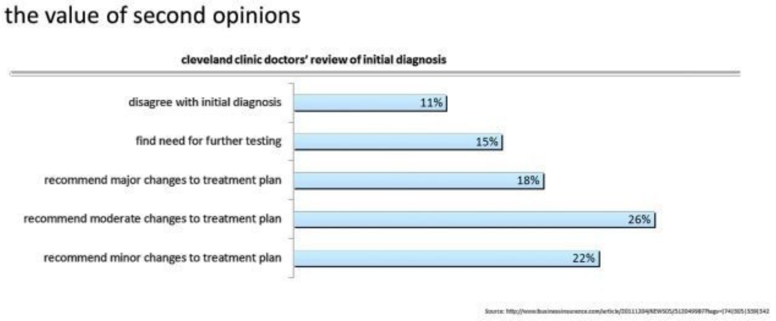
MAYO CLINIC

A Decade of Reversal: An Analysis of 146 Contradicted Medical Practices

Vinay Prasad, MD; Andrae Vandross, MD; Caitlin Toomey, MD; Michael Cheung, MD; Jason Rho, MD; Steven Quinn, MD; Satish Jacob Chacko, MD; Durga Borkar, MD; Victor Gall, MD; Senthil Selvaraj, MD; Nancy Ho, MD; and Adam Cifu, MD

Abstract

Objective: To identify medical practices that offer no net benefits.
Methods: We reviewed all original articles published in 10 years (2001-2010) in one high-impact journal. Articles were classified on the basis of whether they addressed a medical practice, whether they tested a new or existing therapy, and whether results were positive or negative. Articles were then classified as 1 of 4 types: replacement, when a new practice surpasses standard of care; back to the drawing board, when a new practice is no better than current practice; reaffirmation, when an existing practice is found to be better than a lesser standard; and reversal, when an existing practice is found to be no better than a lesser therapy. This study was conducted from August 1, 2011, through October 31, 2012.
Results: We reviewed 2044 original articles, 1344 of which concerned a medical practice. Of these, 981 articles (73.0%) examined a new medical practice, whereas 363 (27.0%) tested an established practice. A total of 947 studies (70.5%) had positive findings, whereas 397 (29.5%) reached a negative conclusion. A total of 756 articles addressing a medical practice constituted replacement, 165 were back to the drawing



Growing complexity of knowledge

- Very slow pace for doctors to acquire new knowledge
- Increased amount of complexity
  - E.g. Coordinating specialists treating a patient is very complex and done using very little technology
- No universally accepted processes and recommendations to make decisions.
  - Those depend on each institution and practitioner
  - 50% of the recommendations made in guidelines based on expert opinion, case studies, or standards of care, not systematic studies

No personalization!

- Clinical Practice Guides are not personalized
  - They might prove negative since they fail to take into account interactions between different diseases (e.g. in older patients)
- Research done on “homogeneous”, healthy subjects
- It is very hard for doctors to “manually” personalize their “recommendations”

What does this have to do with Recsys?

A word on Precision Medicine

Precision medicine

- According to the National Institutes of Health (NIH), precision medicine is:

  "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person."

The NEW ENGLAND JOURNAL of MEDICINE

Perspective
FEBRUARY 26, 2015

A New Initiative on Precision Medicine

Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

"Tonight, I'm launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes — and to give all of us access to the personalized information we need to keep ourselves and our families healthier."

— President Barack Obama, State of the Union Address, January 20, 2015

President Obama has long expressed a strong conviction that science offers great potential for improving health. Now, the President has announced a research initiative that aims to accelerate prog- variability into account — is not new[1]; blood typing, for instance, has been used to guide blood transfusions for more than a century. But the prospect of applying this concept broadly has been is a broad research program to encourage creative approaches to precision medicine, test them rigorously, and ultimately use them to build the evidence base needed to guide clinical practice.

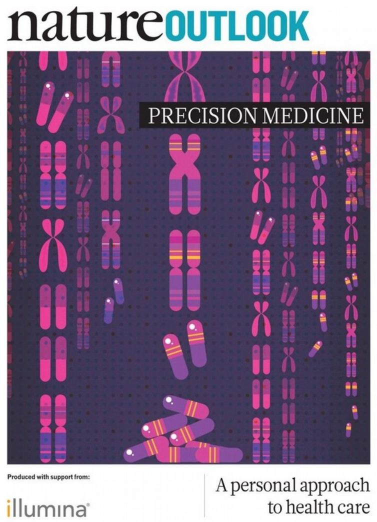
The proposed initiative has two main components: a near-term focus on cancers and a longer-term aim to generate knowledge applicable to the whole range of health and disease. Both components are now within our reach because of advances in basic research, including molecular biol-

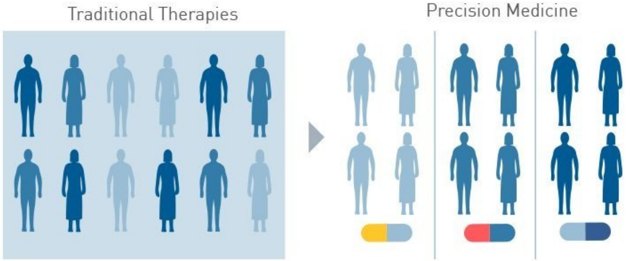
Precision medicine

- Goal: predict more accurately treatment and prevention given a particular disease & group of people

- In contrast to "one-size-fits-all" approach where treatment & prevention are developed for average person

- Term is relatively new, but concept has been around for many years.
  - *E.g. blood transfusion is not given from a randomly selected donor*





Recsys & Medicine

Recommender System (Recsys)

- Recommender systems aim to help users by providing suitable options to execute a task easily and efficiently.
- Such systems learn user behavior by filtering through a large amount of data

Recsys in Health Care

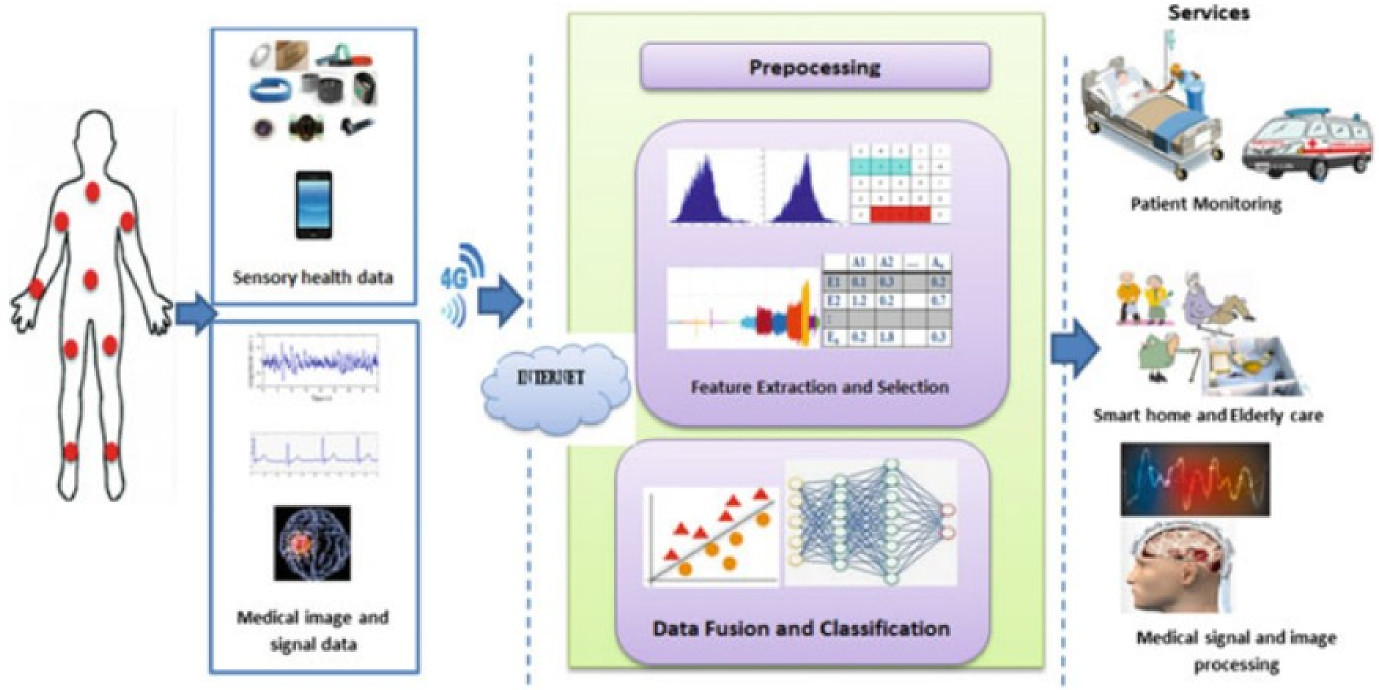


Fig. 2 System architecture of health recommender system

Table 1 Overview of the applications of recommendations for health informatics

Area of applications	Application	Input parameters	Learning techniques
Bioinformatics [4–6]	Drug design	Molecule compounds	Deep neural network
	RNA binding protein Compound protein interaction	Gene RNA/DNA sequences Molecule compounds	Deep belief network
			Deep neural network
Medical imaging [7–9]	Tissue classification Organ segmentation Tumor detection Hemorrhage detection	MRI/CT images Microscopy Hyperspectral images Endoscopy images	Convolutional neural network
			Convolutional deep belief network
			Deep neural network
Pervasive sensing [10–13]	Monitoring of biological parameters Anomaly detection	ECG, EEG Devices implanted	Convolutional neural network
	Human activity recognition	Wearable sensing devices Smartphones Video	Convolutional neural network
			Deep belief network
	Obstacle detection Sign language recognition Hand gesture recognition	RGB-D camera Real-sense camera Depth camera	Convolutional neural network
			Deep belief network
Public health [14, 15]	Lifestyle diseases Infectious disease epidemics	Text messages Social media data Geo-tagged images	Convolutional neural network
			Deep belief network
			Deep neural network

How to improve medicine?

- More/better personalization
- Make better use of (big) data
- Automate processes through algorithms and machine learning
- Better user experience both for patients and doctors

Does this sound familiar?

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Article

Health Recommender Systems: Concepts, Requirements, Technical Basics and Challenges

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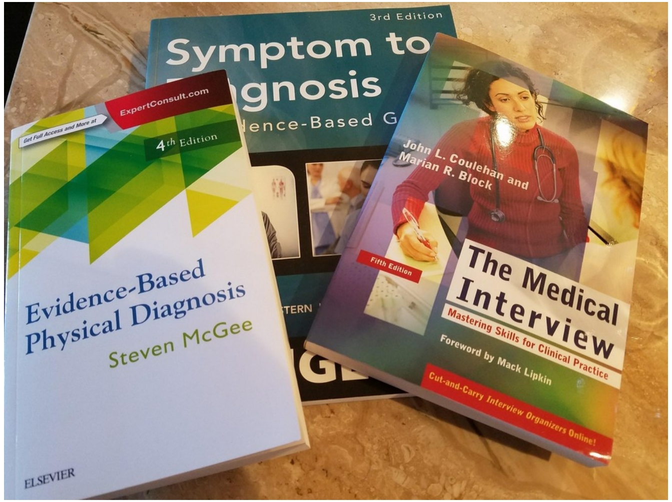
Abstract: During the last decades huge amounts of data have been collected in clinical databases representing patients' health states (e.g., as laboratory results, treatment plans, medical reports). Hence, digital information available for patient-oriented decision making has increased drastically but is often scattered across different sites. As as solution, *personal health record systems* (PHRS) are meant to centralize an individual's health data and to allow access for the owner as well as for authorized health professionals. Yet, expert-oriented language, complex interrelations of medical facts and information overload in general pose major obstacles for patients to understand their own record and to draw adequate conclusions. In this context, *recommender systems* may supply patients with additional laymen-friendly information helping to better comprehend their health status as represented by their record.

Medical Decision Support Systems

Medical Diagnosis

- Diagnosis:
  - *“a mapping from a patient’s data (normal and abnormal history , physical examination , and laboratory data) to a nosology of disease states the process of determining by examination the nature and circumstances of a diseased condition”*
  - *“The knowledge of how to “work up” the patient depends critically on the ability to evoke history, symptoms, and physical examination findings, concurrently with the ability to generate diagnostic hypotheses that suggest how to further refine or pursue the findings already elicited, or to pursue completely different additional findings. In addition, this must be done in a compassionate and cost-effective manner”* (R.A. Miller 1990)



Diagnosis Decision Support Systems

- DDSS
  - A computer - based algorithm that assists a clinician with one or more component steps of the diagnostic process
  - It involves diverse activities:
    - information gathering
    - pattern recognition
    - problem solving
    - Decision-making
    - judgment under uncertainty
    - Empathy
  - Large amounts of highly organized knowledge are necessary
- Two categories
  - General-domain DDSS
  - Specialized DDSS

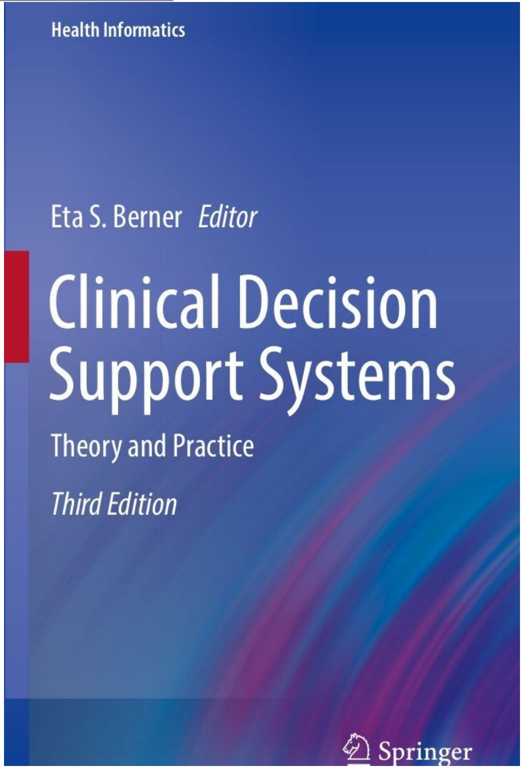
Medical Diagnosis as a Recsys

- Input signals
  - Implicit: Data coming from sensors, labs…
  - Explicit: What does the patient tell us
  - Others: Demographic, family history…
- Algorithms
  - Find what worked for “similar” patients in a “similar” situation
- Output
  - Ranked list with “likely” options
  - Need to also worry about other variables such as acuity, explanations....

Knowledge-based approaches to medical decision systems

Decision/Diagnosis support systems

- They have been developed for decades
- Many early DDSS based on Bayesian reasoning (60s-70s)
  - Bayesian networks (80s-90s)
  - Neural networks (lately)
- Most of them have been developed “manually” with doctors looking at research and manually encoding that into knowledge bases.



Data for Medical Decision Systems

Knowledge bases

- Knowledge base construction
  - Build model from existing medical knowledge
  - E.g. using doctors to read on medical literature and encode “well-established facts”
- Data = Medical Research
  - Ingesting and understanding medical publications can be mostly automated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BMC Medical Informatics and Decision Making

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ExaCT: automatic extraction of clinical trial characteristics from journal publications

Svetlana Kiritchenko, Berry de Bruijn, Simona Carini, Joel Martin and Ida Sim

BMC Medical Informatics and Decision Making 2010 10:56 | https://doi.org/10.1186/1472-6947-10-56

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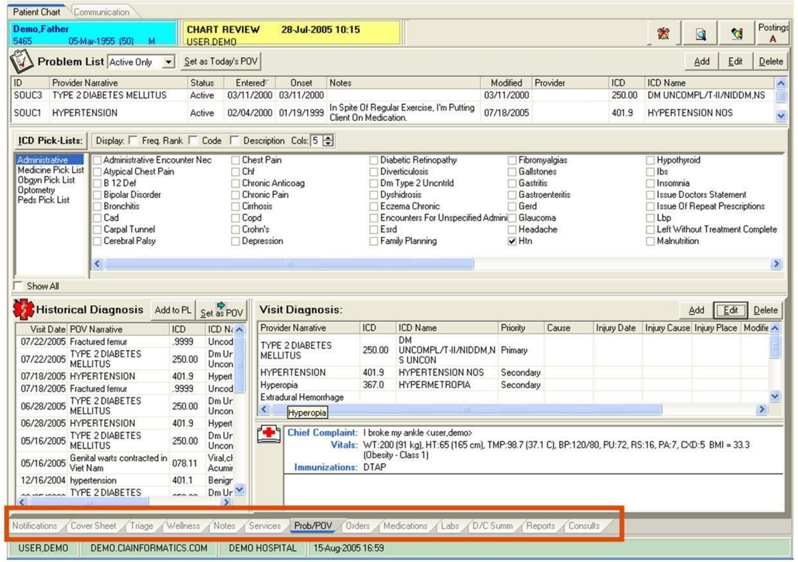
Electronic Health Records

- EHR/EMRs include digital information about patients *encounters* with doctors or the health system



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Extracting Information from Textual Documents in the Electronic Health Record: A Review of Recent Research

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Summary
Objectives: We examine recent published research on the extraction of information from textual documents in the Electronic Health Record (EHR).
Methods: Literature review of the research published after 1995,

Introduction

In the biomedical domain, the rapid adoption of Electronic Health Records (EHR) with the parallel growth of narrative data in electronic form, along

rules or based on statistical methods and machine learning. The information extracted can then be linked to concepts in standard terminologies and used for coding. The information can also be used for decision support and to enrich

Generating Multi-label Discrete Patient Records using Generative Adversarial Networks

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Abstract

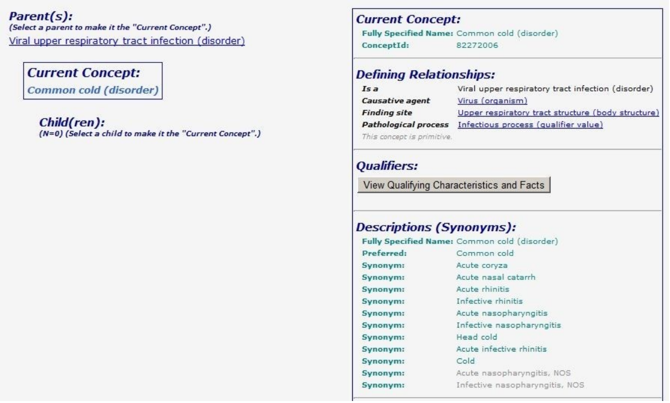
Access to electronic health record (EHR) data has motivated computational advances in medical research. However, various concerns, particularly over privacy, can limit access to and collaborative use of EHR data. Sharing synthetic EHR data could mitigate risk.

In this paper, we propose a new approach, medical Generative Adversarial Network (medGAN), to generate realistic synthetic patient records. Based on input real patient records, medGAN can generate high-dimensional discrete variables (e.g., binary and count features) via a combination of an autoencoder and generative adver-

Ontologies

- Snomed Clinical Terms
  - Computer processable collection of medical terms providing codes, terms, synonyms and definitions used in clinical documentation and reporting.
  - Considered to be the most comprehensive, multilingual clinical healthcare terminology
  - Primary purpose: encode the meanings that are used in health information & support effective clinical recording of data with the aim of improving patient care.
  - It provides the core general terminology for electronic health records.
  - It includes: clinical findings, symptoms, diagnoses, procedures, body structures, organisms and other etiologies, substances, pharmaceuticals, devices and specimens.

SNOMED CT
The global language of healthcare



Ontologies

- ICD-10
  - 10th revision of the **I**nternational Statistical **C**lassification of **D**iseases and Related Health Problems (ICD), a medical classification list by the World Health Organization (WHO)
  - It contains codes for diseases, signs and symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or diseases
  - The code set allows more than 14,400 different codes and permits the tracking of new diagnoses.

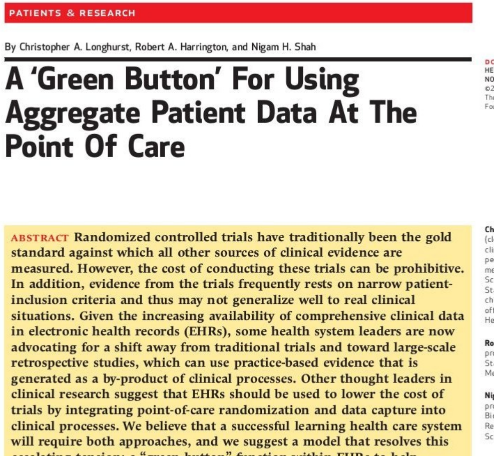
Ontologies

- UMLS (1986)
  - Designed and is maintained by the US National Library of Medicine, updated quarterly, free
  - Compendium of many controlled vocabularies in the biomedical sciences.
  - Provides mapping structure among vocabularies
  - Allows to translate among the various terminology systems
  - It can be interpreted as a thesaurus and ontology of biomedical concepts.
  - It provides tools for natural language processing.
  - Intended for developers of systems in medical informatics.

Unified Medical Language System® (UMLS®)

Combining and aggregating data

- At the end, what you need is a way to process and aggregate all these different sources of data either manually (expert systems) or algorithmically (ML)


PATIENTS & RESEARCH

By Christopher A. Longhurst, Robert A. Harrington, and Nigam H. Shah

A 'Green Button' For Using Aggregate Patient Data At The Point Of Care

ABSTRACT Randomized controlled trials have traditionally been the gold standard against which all other sources of clinical evidence are measured. However, the cost of conducting these trials can be prohibitive. In addition, evidence from the trials frequently rests on narrow patient-inclusion criteria and thus may not generalize well to real clinical situations. Given the increasing availability of comprehensive clinical data in electronic health records (EHRs), some health system leaders are now advocating for a shift away from traditional trials and toward large-scale retrospective studies, which can use practice-based evidence that is generated as a by-product of clinical processes. Other thought leaders in clinical research suggest that EHRs should be used to lower the cost of trials by integrating point-of-care randomization and data capture into clinical processes. We believe that a successful learning health care system will require both approaches, and we suggest a model that resolves this

ML for Medical Decision Systems

Health graphs

SCIENTIFIC DATA

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SUBJECT CATEGORIES
» Data mining
» Diagnosis
» Epidemiology
» Outcomes research

Building the graph of medicine from millions of clinical narratives

Samuel G. Finlayson, Paea LePendu & Nigam H. Shah

Electronic health records (EHR) represent a rich and relatively untapped resource for characterizing the true nature of clinical practice and for quantifying the degree of inter-relatedness of medical entities such as

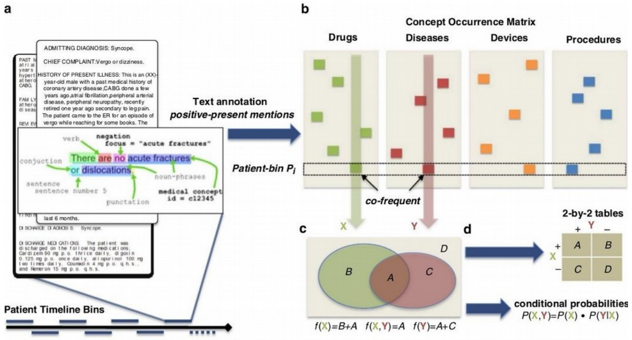

Figure 1. Workflow Architecture. The architecture of our workflow starts with (**a**) patient notes that are grouped together based on their nearness in time. Given the patient timeline bins, clinical terms are recognized from the notes and recorded into (**b**) the clinical concept occurrence matrix, which is scanned for (**c**) counting pairwise the frequency and co-frequency of concepts. This data can be used to calculate (**d**) contingency tables and Bayesian probability estimates. For example, the concept X has a frequency of *f*(X) and is pairwise co-frequent with concept Y exactly *f*(X,Y) times.

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Learning a Health Knowledge Graph from Electronic Medical Records

Received: 3 March 2017
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Published online: 20 July 2017

Maya Rotmensch[1], Yoni Halpern[2], Abdulhakim Tlimat[3], Steven Horng[3,4] & David Sontag[5,6]

Demand for clinical decision support systems in medicine and self-diagnostic symptom checkers has substantially increased in recent years. Existing platforms rely on knowledge bases manually compiled through a labor-intensive process or automatically derived using simple pairwise statistics. This study explored an automated process to learn high quality knowledge bases linking diseases and symptoms directly from electronic medical records. Medical concepts were extracted from 273,174 de-identified patient records and maximum likelihood estimation of three probabilistic models was used to automatically construct knowledge graphs: logistic regression, naive Bayes classifier and a Bayesian network using noisy OR gates. A graph of disease-symptom relationships was elicited from the learned parameters and the constructed knowledge graphs were evaluated and validated, with permission, against Google's manually-constructed knowledge graph and against expert physician opinions. Our study shows that direct and automated construction of high quality health knowledge graphs from medical records using rudimentary concept extraction is feasible. The noisy OR model produces a high quality knowledge graph reaching precision of 0.85 for a recall of 0.6 in the clinical evaluation. Noisy OR significantly outperforms all tested models across evaluation frameworks ($p < 0.01$).

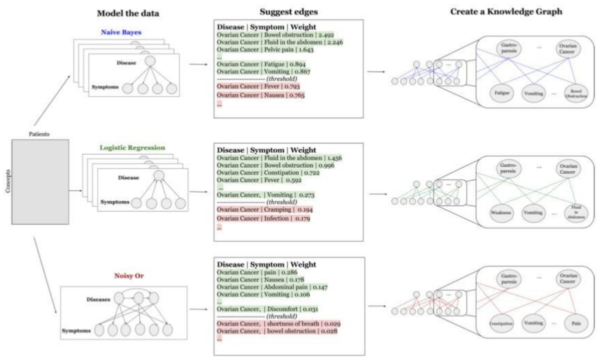

Figure 2. Workflow of modeling the relationship between diseases and symptoms and knowledge graph construction, for each of our 3 models (naive Bayes, logistic regression and noisy OR).

NLP

- Understanding what doctors say
- Understanding what patients say

Proceedings of Machine Learning for Healthcare 2017 JMLR W&C Track Volume 68

Diagnostic Inferencing via Improving Clinical Concept Extraction with Deep Reinforcement Learning: A Preliminary Study

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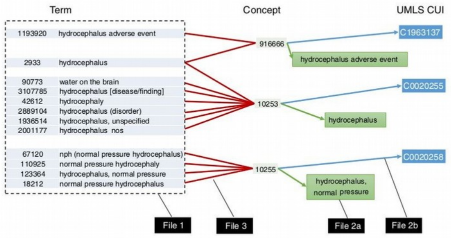


Figure 2. Mappings among terms and concepts. The figure explains the mappings that can be used to decode the frequency files stored in records 1 and 2. We use a subset of terms related to 'hydrocephalus' to demonstrate the mapping of terms (File 1) to concepts and UMLS CUIs. Terms map onto concepts in a many-to-many fashion (File 3). Concepts map onto CUIs in a one-to-one fashion (File 2b) and have an associated string for human readability (File 2a).

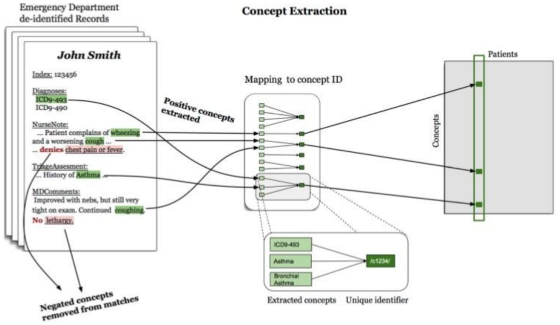
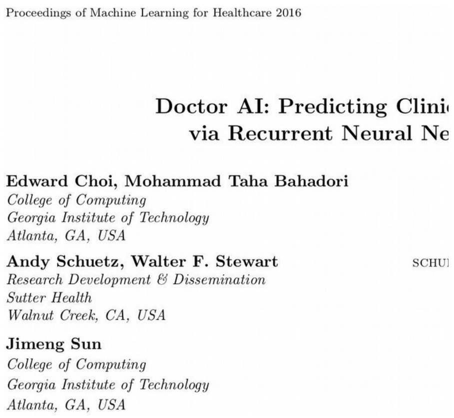


Figure 1. Concept extraction pipeline. Non-negated concepts and ICD-9 diagnosis codes are extracted from Emergency Department electronic medical records. Concepts, codes and concept aliases are mapped to unique IDs, which in turn populate a co-occurrence matrix of size (Concepts) × (Patients).

Diagnostic Systems

- Building diagnostic systems from data through ML


Proceedings of Machine Learning for Healthcare 2016

Doctor AI: Predicting Clini
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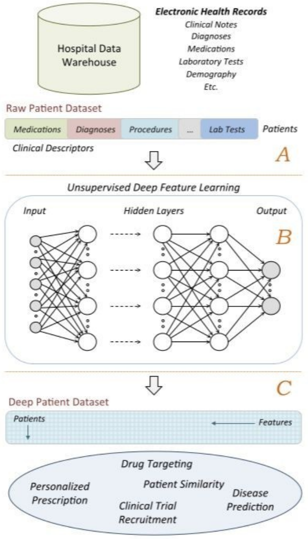
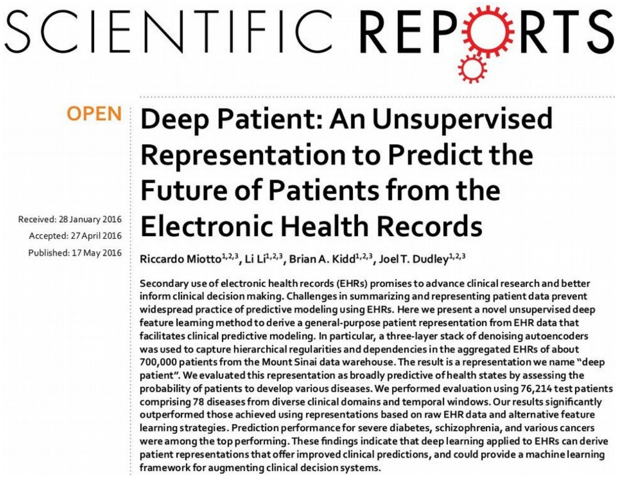


Figure 1. Conceptual framework used to derive the deep patient representation through unsupervised deep learning of a large EHR data warehouse. (**A**) Pre-processing stage to obtain raw patient representations from the EHRs. (**B**) The raw representations are modeled by the unsupervised deep architecture leading to a set of general and robust features. (**C**) The deep features are applied to the entire hospital database to derive patient representations that can be applied to a number of clinical tasks.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Deep Patient: An Unsupervised Representation to Predict the Future of Patients from the Electronic Health Records

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Published: 17 May 2016

Riccardo Miotto[1,2,3], Li Li[1,2,3], Brian A. Kidd[1,2,3], Joel T. Dudley[1,2,3]

Secondary use of electronic health records (EHRs) promises to advance clinical research and better inform clinical decision making. Challenges in summarizing and representing patient data prevent widespread practice of predictive modeling using EHRs. Here we present a novel unsupervised deep feature learning method to derive a general-purpose patient representation from EHR data that facilitates clinical predictive modeling. In particular, a three-layer stack of denoising autoencoders was used to capture hierarchical regularities and dependencies in the aggregated EHRs of about 700,000 patients from the Mount Sinai data warehouse. The result is a representation we name "deep patient". We evaluated this representation as broadly predictive of health states by assessing the probability of patients to develop various diseases. We performed evaluation using 76,214 test patients comprising 78 diseases from diverse clinical domains and temporal windows. Our results significantly outperformed those achieved using representations based on raw EHR data and alternative feature learning strategies. Prediction performance for severe diabetes, schizophrenia, and various cancers were among the top performing. These findings indicate that deep learning applied to EHRs can derive patient representations that offer improved clinical predictions, and could provide a machine learning framework for augmenting clinical decision systems.

Challenges

- Algorithmic: e.g. combining expert rule-based and ML
- Data: quality, sparsity, and bias in data
- UX: trustworthiness and engagement of the system, incentives…
- Legal
- …

It’s about time we overcome all of these.

Conclusions

- Medicine/healthcare is one of the areas in society that can benefit most from technology in general and algorithmic approaches in particular
- Medicine has many similarities to recommender systems
  - Importance of data (both big and small)
  - Content and collaborative approaches
  - Importance of UI/UX (e.g. user understanding, feedback, and explanations)
  - Evaluation has to be sensitive to overall optimization problem
- Huge opportunity, great mission: looking forward to many advances that will save millions of lives in the next few years

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