Workshop Introduction
Putting the Pieces Together: Precision Medicine Discovery from Electronic Health Records

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Precision Medicine

The right medicine

And the right intervention

The right patient

The right dose

The right time

Also remember we are moving to drug development based on genetic variation

A Key to Precision Medicine

- We collect a tremendous amount of information about health and disease through **electronic health records**
  - Diagnoses
  - Clinical Lab Measurements
  - Medications
  - In patient and out patient

- What if we use these information to help inform better patient treatment?

http://www.brimg.net/images/doctor-using-mobile-chart-checking-patient-corbis_573x300.jpg
http://ihealthtran.com/wordpress/wp-content/uploads/2012/11/EHR-Health-IT.jpg

Integrating EMRs into Genomic Research

Use of EMRs in medicine

Early 1990's

Sequenced the human genome

2001

Improved technologies for biomedical analysis

~ 2005

NHGRI eMERGE Initiative

2007

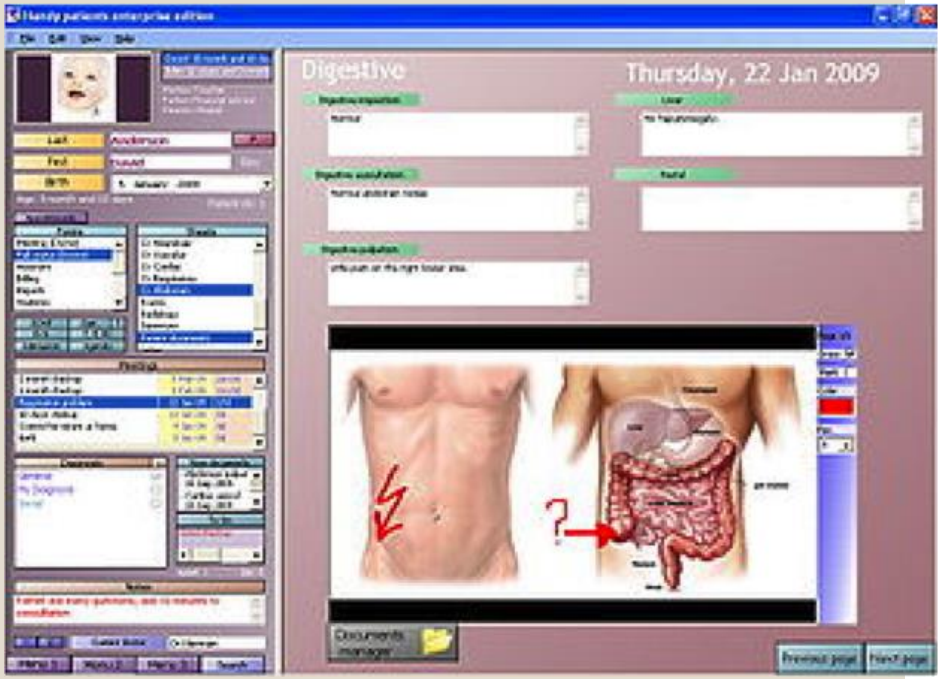
Tools for analyzing large datasets

Now

Janina M. Jeff, PhD, MS

ELECTRONIC HEALTH RECORDS (EHRS)

- Electronic Health Records (EHRs)
- Electronic version of a patients medical history
  - maintained by the provider over time
  - demographics, progress notes, problems, medications, vital signs, past medical history, immunizations, laboratory data, biomarkers, and radiology reports



"EHRs will enable providers to make better decisions and provide better care. "

Electronic Health Record (EHR) Linked to Genetic Data

- Success in research discovery with de-identified patient electronic health records (EHR) linked to de-identified genetic data
  - Identification of novel genetic associations

- Genetic Data
  - Single nucleotide polymorphisms (SNPs)
  - Common frequency variants
  - Genome-wide association studies
  - Pharmacogenomics

- EHR
  - Wide range of patient derived data

Illustration: iStockphoto

Electronic Health Record (EPIC/Clarity)

- Ambulatory (Outpatient)
- Inpatient (Hospital Admissions)
- Emergency Department
- Medication Orders
- Lab (Orders and Results)
- Imaging Orders
- Procedures
- Diagnosis information
- Demographics
- Patient History (Social, Surgical, Medical, etc.)
- Problem List

Disparate Data Sources

- Cardiology Databases (Xcelera [1991 forward], MUSE [1980 forward], Echo [1991 forward], Apollo [1999 forward])
  - Cardiovascular Imaging (MR/CT)
  - Electrocardiogram
  - Echocardiogram
  - Surgical and Catheterization
- Radiology (RIS) [1997 forward]
  - Pre-procedure questions
  - Radiology Reports
- DEXA [1998 forward]

Phenotypic Algorithm Development

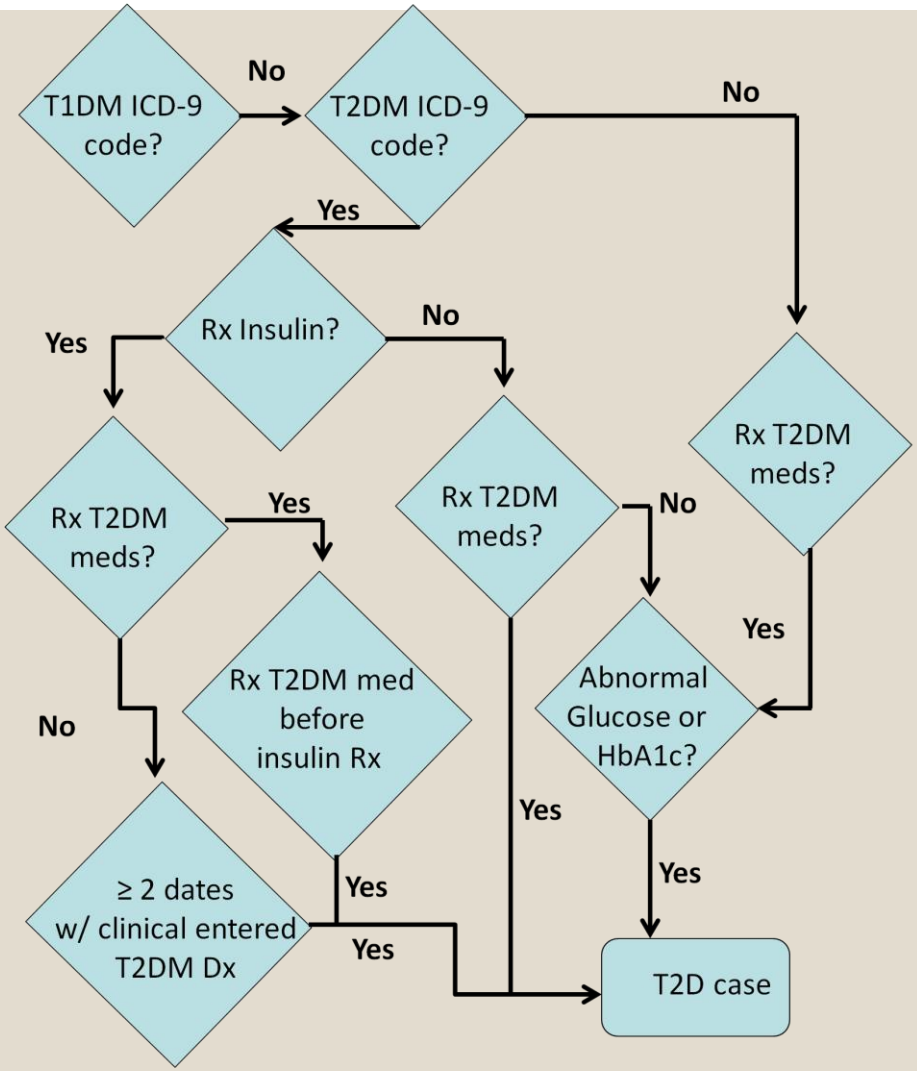
- Terminology
  - Using International Classification of Disease codes (ICD-9, ICD-10)
  - Procedural Codes (CPT)
  - Problem lists (Historical Codes, V,T,E codes)
  - Clinical Laboratory Values
  - Pharmacologic Data
  - Vital Signs
  - Structured Billing Text and Notes

- Note: Variability in these data exists across multiple EHR platforms

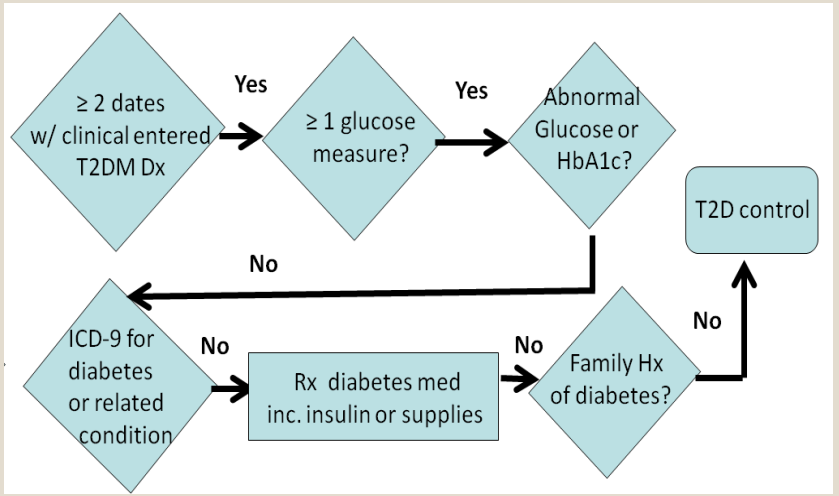
Developing a Phenotypic Algorithm

- Using multiple pieces of information to define case/control status, or a quantitative phenotypic measure
  - What is your phenotype of interest?
  - How can this phenotype be optimally used for increased power in a large-scale 'omic analysis?
  - Who are the individuals that will be affected by this disease or will have this phenotype?
  - Is it a case/control phenotype, quantitative measure?
  - What are medications, comorbidities, other diseases, surgeries that might affect your phenotype or measure?
    - Example: lipid levels after drug treatment suggesting an individual has "normal" lipid levels, impacting who you define as "high lipid levels"
    - Example: patient incorrectly defined as a control due to treatment radically changing their patient medical record, such as gastric bypass surgery resulting in type-2 diabetes reversal
    - Example: patient incorrectly defined as a "case" when their condition is a a result of surgery

Phenotypic Algorithm: Flow Chart

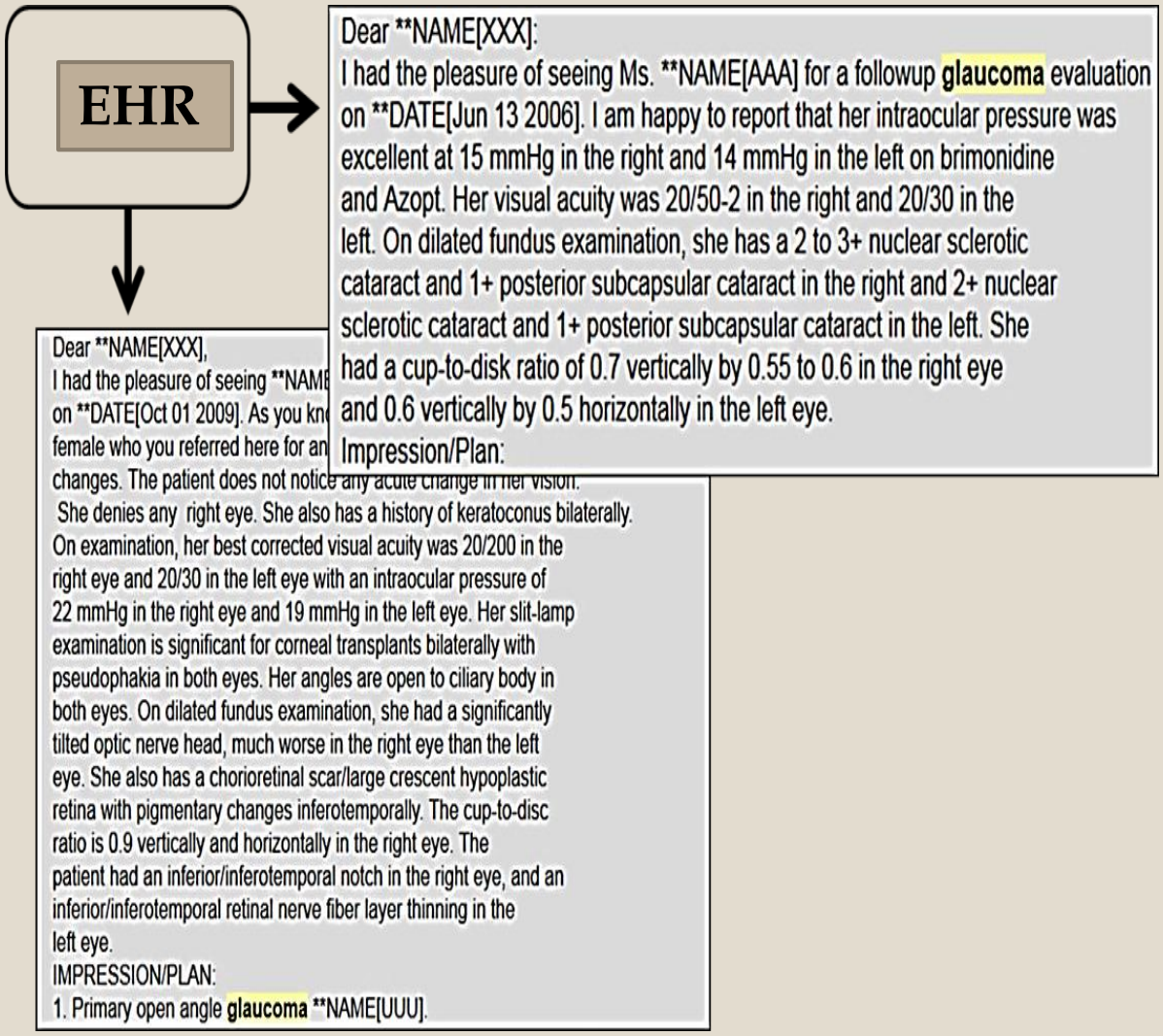


Case definition



Control definition

Clinical notes/communications allow for Indirect Verification



Developing a Phenotypic Algorithm

- How do I know it works?
  - Use algorithm to define group of cases and controls and evaluate PPV and NPV
    - Chart review
  - **PPV: Positive Predictive Value** is the probability that subjects with a positive screening test truly have the disease
    - Iteratively refine case definition through partial manual review until case definition yields PPV ≥ 95%
  - **NPV: Negative Predictive Value** is the probability that subjects with a negative screening test truly don't have the disease
    - For controls, exclude all potentially overlapping syndromes and possible matches, iteratively refine such that NPV ≥ 98%

More Resources?

- PheKB (https://phekb.org/)
  - Documentation and versioning of validated phenotype algorithms
    - Implementation details
  - Can validate existing phenotype algorithms in a different EHR
  - Collaborate on phenotypic algorithm develpment