The Future of the Electronic Health Record

Gerry Higgins, Ph.D., Johns Hopkins
Topics to be covered

• **Near Term Opportunities**: Commercial, Usability, Unification of different applications.

• **‘OMICS’**: The patient’s entire genome to be included in the EHR, along with nosology-specific annotation, proteomics, metabolomics. Enormous storage requirements will be required.

• **Pharmacogenomic Clinical Decision Support** system for 30-50% of all prescribed drugs.

• **Personal Health Records (PHI)** will become a venue for wealthy patients to access their medical records, but in a strictly controlled manner.

• **The EHR as an ‘On-Demand’ learning system** for cognitive and psychomotor skills, as well as certification.
The Future - Commercial

- Bigger IT companies will buy EHR vendors – consolidation.

Microsoft Health Solutions > Amalga
Allscripts > Eclipsys
IBM > Datacap
Oracle > Epic? Cerner?
HP and McKesson
The Future of the EHR

- Vendors that don’t increase the **usability** of their current EHR offerings won’t survive.
Security of mHealth EHRs / PHRs

- Mobile EHRs will be hacked, stolen or lost, causing increased security concerns and enhancements for all EHRs.
Unification of classification and ontology will become standard, either through vendor cooperation and/or federal regulation.

Examples:

- Unified Medical Language System® (UMLS)
- Gene Ontology (GO)
- Systematized Nomenclature of Medicine (SNOMED)
- Foundational Model of Anatomy (Univ. Washington)
- Transparent Access to Bioinformatics Information Sources (TAMBIS)
Unification of the ‘Universe of Medication Applications’
(courtesy of Agilis, LLC)
The ‘new genomics’

A Patient’s Genomic Data has to be Embedded in Overall Health Context

Family History:
- First degree relative assessment
- Ancestry
  *for:*
- Common, multifactorial disorders, as well as Mendelian disorders

EHR:
- Clinical data repository, test results, radiologic images, etc.
- Longitudinal health record
- Age, sex, vitals
- Nursing documentation
- Pharmacy, including medication history

Lifestyle:
- Stress
- Diet and nutritional status
- Exercise
- Tobacco, alcohol, drugs

Personal Genome:
- Mendelian traits
- Common, complex traits due to common *and* rare variants
- Pharmacogenomic profile
- Copy Number Variants

PATIENT
The ‘new genomics’ – molecular biology

Human Genome: ~25,000 genes

Transcriptome

Messenger RNA splicing: ~100,000 transcripts

RNA transcripts:

Proteome

Proteins: ~2M normal, blocked with iRNAs, modified

Epigenetics

Interference RNA

Gene therapy using microRNAs
# Aspects of some of the patient’s genome to be included in the EHR

## Mendelien inheritance (monogenic):
- Trait is passed down generations in a classical genetic manner. If you inherit the gene, you have at least a 25% chance of getting the disease.

## Common, complex polygenic diseases and traits:
- Common variants that increase inherited susceptibility to a disease (non-classical) – easy to detect.
- Rare variants – hard to detect.

## Pharmacogenomic Clinical Decision Support:
- The right drug prescribed for the right patient, at the right dose, based on their genomic profile.
Aspects of the patient’s genome to be included in the EHR

Genome Wide Association Studies (GWAS):

• A rapid scan of markers across the complete genomes of many people to find genetic variations associated with a particular disease. Such studies are useful in finding genetic variations for common, complex diseases, such as asthma, cancer, Type 2 diabetes, heart disease and mental illnesses.

• Sample size usually is 100,000 – 2,000,000 Single Nucleotide Variants (SNPs), and involve 100 – 10,000+ individuals.

• However, the use of SNP analysis in GWAS has missed markers for several common diseases such as Type 2 diabetes. This may because this and other complex diseases have many rare variant genes.
Aspects of the patient’s genome to be included in the EHR

Problem: There are 1500 medically relevant genes – ones that are clinically ‘actionable’ (apart from PGx variants). However, very few mutations that have been identified to date that convey risk of inherited disease of more than 1-2 fold that of the general population, yet we know that millions of such disease alleles exist.
The ‘new genomics’

- First human genome sequenced by Dr. Craig Venter and associates – NIH followed next, and both papers were published in 2001. About 3 billion base pairs.

- The number of genes has been estimated to be around 25,000, but because these can be differentially processed (e.g., mRNA splicing, iRNA) - some organs such as the brain contain over 100,000 proteins.

- The ‘exome’ is the entirety of the protein-encoding exons of the genome. Not all disease-causing mutations or problems arise from the exome.
Cost of Patient Genome Sequencing, Storage & Analysis

Units = $1000

Adapted from George M. Church, Personal Genomes, Cold Spring Harbor Lab
The ‘new genomics’

BIGGEST CHALLENGES FOR THE ‘GENOME-ENABLED’ ELECTRONIC HEALTH RECORD

- Providing Clinical Decision Support for the Clinician to Make Diagnosis in a Rapid, Accurate and Comprehensible Manner

- The Cost of Storing the Entire Patient Genome in the EHR, or even secondary, extracted genomic, proteomic and metabolomic data

- Providing Genomic Education for Clinicians about the ‘New Genomics’
The Promise of Pharmacogenomics (PGx)

“The right drug prescribed for the right patient based on their genetic susceptibility profile.”

- All patients with the same diagnosis
  - No Response or Toxic Response
    - Treat with alternative drug or dose
  - Responsive, No Adverse Events
    - Treat with conventional drug or dose
  - SNP Analysis, Gene Microarray
Solution: PGx Clinical Decision Support

- Information overload
- Limited time with patients
- How can the EHR help?

PGx Clinical Decision Support
Pharmacogenetics (PGx)

- **Pharmacogenetics**: The study of varying responses to drugs between individuals, and the determination of the specific genetic mutations underlying these variations. *First specialties:*
  - Oncology
  - Cardiovascular disease
  - Psychiatry

- **Pharmacogenomics**: The study of varying responses to drugs between individuals, based on whole genome analysis, that underlies these variations.
PGx: Integration with the EHR

Challenges

- Empower patients
- Educate physicians
- Translate scientific discovery into clinical practice
PGx: Challenges in Clinical Practice
Patients Respond Differently to Drugs – “One Size Does Not Fit All”

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Depressants (SSRI’s)</td>
<td>38%</td>
</tr>
<tr>
<td>Asthma Drugs</td>
<td>40%</td>
</tr>
<tr>
<td>Diabetes Drugs</td>
<td>43%</td>
</tr>
<tr>
<td>Arthritis Drugs</td>
<td>50%</td>
</tr>
<tr>
<td>Alzheimer’s Drugs</td>
<td>70%</td>
</tr>
<tr>
<td>Cancer Drugs</td>
<td>75%</td>
</tr>
</tbody>
</table>

Percentage of the patient population for which a particular drug in a class is ineffective, on average
The Challenge of Accurate Warfarin Dosing

- ~ 2 million people in the US receive warfarin (Coumadin®) every year; Ranked in the top 4 of medications causing Adverse Events (AE).

- Differential response between individuals partly based on genetic heterogeneity. A patient’s clinical information is 12-17% accurate in dosing – addition of the alleles of the VKORC1 and CYP2C9 genes brings this to ~60% accuracy.
Warfarindosing.org: What is It?

- 26 algorithms
  - Days 1 – 10
  - Clinical and Genetic
  - Indications

- Drug interactions
  - Amiodarone
  - Statins
  - Azoles, etc.

- Randomize and Blind for clinical trials
  - Clinical vs. Genetic Algorithms
## Clinical Info*<br>

<table>
<thead>
<tr>
<th>Gene</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VKORC1-1639/3673</strong></td>
<td>GG (warfarin insensitive)</td>
</tr>
<tr>
<td><strong>CYP4F2 V433M</strong></td>
<td>Not available/pending</td>
</tr>
<tr>
<td><strong>GGCX rs11676382</strong></td>
<td>Not available/pending</td>
</tr>
<tr>
<td><strong>CALU</strong></td>
<td>Not available/pending</td>
</tr>
<tr>
<td><strong>CYP2C9*2</strong></td>
<td>TT (homozygous mutant)</td>
</tr>
<tr>
<td><strong>CYP2C9*3</strong></td>
<td>AA (wildtype)</td>
</tr>
<tr>
<td><strong>CYP2C9*5</strong></td>
<td>Not available/pending</td>
</tr>
<tr>
<td><strong>CYP2C9*6</strong></td>
<td>Not available/pending</td>
</tr>
</tbody>
</table>
• Brian Gage, M.D., M.S., Washington University.
• Kraig Robson, M.S., Isodynamic LLC - Web services and hosting.
• Ken Kawamoto, M.D., Ph.D., Duke University.
Major Issue for CDSS – Usability

- Major flaw of most CDSS in usability
- Another challenge is how to update information rapidly
- How to integrate into workflows?
- How to prevent “alert fatigue”?
- How to present complex information so that it can be:
  - Quickly interpreted
  - Quickly communicated
  - Not take up the entire 15 minute visit
Major business model – CDSS in the EHR: Current Generation: Manual, labor intensive

Medical publishing / informatics company

Thousands of medical experts that ‘scour’ the medical literature

Provide to EHR Vendors
Major business model – CDSS in the EHR: Next Generation: Automated with Oversight

“Cloud of Medical and Scientific Information”

Expert Curation

Ontology-based Rule Sets

Provide to EHR Vendors
CDSS in the EHR: Continuous Learning During Performance

Assess Competency

Assimilate Data and Make Decision

Present Simulated Patient Case in EHR

Assemble New Integrated Patient Data into ‘Dummy Case’

Measure Diagnostic Decisions

Real-Time Data Display in EHR

Adapted from William Stead