Developing Standards and Infrastructure to Enable Genetic Aware Clinical Decision Support within the EHR Ecosystem

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Disclosure

• GeneInsight technology discussed in this presentation has been licensed to a company named GeneInsight Inc., the stockholders of which are Partners HealthCare System and Sunquest.

• Sandy Aronson is an employee of Partners HealthCare.
What is the cause of these symptoms?

What treatments will help?

How much risk is present?

How aggressively should I manage this patient?
How Do We Introduce Genetics to the Broader Community?

- 3 Billion Base Pairs of DNA Per Person
- 3-5 Million Variants Per Patient
- 22,000 Genes

Big Data Shock and Awe
Shocked and Awed

This train is moving 500 mph ....

But my healthcare training is moving at 2 mph.

Do you know what happens when you try to dock a 500 mph train to a 2 mph train?
The complexity and sophistication of this is incredible ....

But you get that I only have 15 minutes with each patient, right?
Shocked and Awed

This gets me so excited about the future....

But is it really ready for prime time?
I am glad that a lot of smart people are thinking about this ....

But is there really any way that I am actually going to be able to apply it for my patients?

Is there any way I am going to be able to contribute to making this happen?
We Need to Prove We Collectively Can Handle This
Our Clinicians Need

- Distilled, accurate, understandable genetic test results
- Results that are well integrated into the EHR
- Alerts when significant new information emerges on a previous genetic finding that could help one of their patients
- Confidence that they will be able to understand, apply and manage results
Typical Situation

• Genetic test results are scattered through EHR

• Most results are not structured, organized or adequately interpreted for clinical use at point of care

• Significance of genetic variants change over time and clinicians are not updated as new knowledge emerges

• Most genetic findings received can not be used by electronic clinical decision support
Typical Health Information Technology

Clinical Decision Support Engine

Rules Generated Outside of Clinical Flow

Clinical Decision Support in this Environment Evolves Too Slowly

Transactions but does not Refine Rules
Optimally Linking Clinicians and Laboratories is Key
Institute of Medicine
EHR Action Collaborative

• Assemble the right organizations

• Identify areas of agreement

• Initiate inter-institutional project coordination
Objective: Build the Foundation

Framework for Increasing Support for Genetics in the EHR Ecosystem

- PGx Use Case Patterns
- Germline Use Case Patterns
- Somatic Use Case Patterns

Initial PGx Use Case Types
- Specific Example

Initial PGx Use Case Types
- Specific Example
# Use Cases Types

<table>
<thead>
<tr>
<th>#</th>
<th>Use Case Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Incorporating Genetic Results into EHR User Interfaces</td>
</tr>
<tr>
<td>2</td>
<td>Adding genetic tests in order sets</td>
</tr>
<tr>
<td>3</td>
<td><em><em>Clinical Decision Support (CDS) identifies when a test should be ordered (pre-test alert</em>)</em>*</td>
</tr>
<tr>
<td>4</td>
<td><em><em>CDS identifies when a drug order is inconsistent with a test result (post-order alert</em>)</em>*</td>
</tr>
</tbody>
</table>

* Note pre and post order status refers to the status of the test order as opposed to the drug order
Specific Type 4 Use Case Example
Abacavir Hypersensitivity

Warn clinicians who prescribe Abacavir to a patient with a genetic test result that indicates they will be hypersensitive.
Interdependency

Providers ➔ Data ➔ Labs
Interdependency

Interoperability and functionality

Providers → Labs

Data

EHR Vendors
LIS Vendors
Supporting Vendors
Interdependency

Data

Interoperability and functionality

Provider

Labs

Cooperation / Interfaces

EHR Vendors

LIS Vendors

Supporting Vendors
Interdependency

Funding / Reimbursement Environment that Makes this Possible

Providers

Labs

Interoperability and functionality

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Supporting Vendors

Standards and Ontologies

Input

Standards & Ontology Organizations

Gov Agencies

Cooperation / Interfaces
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Interoperability and functionality

Proof of what is possible/helpful

Gov Agencies

Cooperation / Interfaces

EHR Vendors

LIS Vendors

Supporting Vendors

Standards and Ontologies

Input

Standards & Ontology Organizations
Action Collaborative Membership

Mark Adams, Good Start Genetics
Gil Alterovitz, Harvard Medical School
Sandy Aronson, Partners HealthCare
J.D. Nolen, Cerner
Brian Anderson, athenahealth
Jane Atkinson, NIDCR
Larry Babb, Partners HealthCare
Dixie Baker, Martin, Blanck and Associates
Gillian Bell, Moffitt Cancer Center
Chris Chute, Johns Hopkins University
Chris Coffin, Invitae
Mauricio De Castro, U.S. Air Force
Carol Edgington, McKesson
Laurel Estabrooks, Soft Computer Corporation
Robert Freimuth, Mayo Clinic
Geoff Ginsburg, Duke University
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Ira Lubin, CDC
Elaine Lyon, ARUP Laboratories
John Mattison, Kaiser Permanente
Larry Meyer, VA
Blackford Middleton, Vanderbilt University
Doug Moeller, McKesson
Scott Moss, Epic
James O’Leary, Genetic Alliance
Erin Payne, Northrop Grumman
Brian Pech, Kaiser Permanente
Teji Rakhra-Burris, Duke University
Priyadarshini Ravindran, Allscripts
Mary Relling, St. Jude Children's Research Hospital
Wendy Rubinstein, NCBI
Hoda Sayed-Friel, Meditech
Megan Schmidt, Sunquest Information Systems
Jud Schneider, NextGx Dx
Sam Shekar, Northrop Grumman
Brian Shirts, University of Washington
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Charles Tuchinda, First Databank
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Marc Williams, Geisinger
Grant Wood, Intermountain Healthcare
Interdependency

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Cooperation / Interfaces

Standards & Ontology Organizations
What Really Happens When Folks Come Together

- Providers
- Labs
- EHR Vendors
- LIS Vendors
- Supporting Vendors
- Standards & Ontology Organizations
- Gov Agencies

Cooperation / Interfaces
The Overarching Problem Remains Large

Framework for Increasing Support for Genetics in the EHR Ecosystem

PGx Use Case Patterns
Germline Use Case Patterns
Somatic Use Case Patterns

Initial PGx Use Case Types
Initial PGx Use Case Types

Specific Example
Specific Example
We Need to Move More Then Data
We Need to Move Knowledge
Laboratories Need

- Mechanisms to storage, organize and manage genetic knowledge and report histories
- High throughput ways to generate quality, consistent and concise reports
- Mechanism for collaborating with other laboratories
- Assistance communicating with clinicians
Literature provides *headstart* on these.

Clinical lab will likely be the first to encounter these.

*Only One Option*

Establish a continuous learning process that operates in the clinical space.
Laboratory – Clinic Integration

GenelInsight Lab
- Reporting Engine
- Laboratory Knowledgebase
- Case Repository

GenelInsight Clinic
- Patient Genomic Profile Repository
- Alerting Engine
- EHR Connectivity

Supports Molecular Diagnostic Labs

Supports Clinicians Who Order Genetic Tests

Transactional and Knowledge Integration is Needed
GeneInsight Report Drafting Engine

Templates Defining High Level Scenarios

Identified Variants
Order Information

Auto-drafted Reports for Geneticist / Pathologist / GC Review

Case Specific
Variant Specific
Generalized to Scenarios

Knowledge Base Containing Variant and Gene Classifications as well as Supporting Evidence
Knowledge Base Containing Variant and Gene Classifications as well as Supporting Evidence

Engine Embedded in Core Transaction Flow

Templates Defining High Level Scenarios

Identified Variants

Order Information

Nothing makes it to here ...

... unless it goes through here ...

... so this must be updated as part of the reporting process itself

Auto-drafted Reports for Geneticist / Pathologist / GC Review
The Initial Bargain

Laboratories agrees:
- Curate new variants in real time as part of reporting process
- Expend the effort required to maintain their knowledgebase

Laboratories get:
- Speed: Reports with previously curated variants autodraft
- Consistency: Autodrafting decreases variability
- Quality: Knowledge is organized and iteration is easier
- Better reports: Templates can produce clear, concise, specific reports

But this is just the beginning ...
Continuous Learning as a Biproduct

Templates Defining High Level Scenarios

Identified Variants

Order Information

Knowledge Base Containing Variant and Gene Classifications as well as Supporting Evidence

Newly recorded knowledge informs future reports and...

...provides updated information to clinicians for existing patients!

Auto-drafted Reports for Geneticist / Pathologist / GC Review
Challenge in Personalized Medicine

Constant Flow of Cases

Geneticist Constantly Signs out Cases

Leveraged and maintained as each case is signed out

Evolving Knowledgebase

Treating Clinicians Consume Reports

Continuous Grows

Case History

Updating Reports When New Information Emerges on a Variant is Critical ... But Unreimbursed

Evolving Knowledgebase
Driving Cost Out of Increased Quality

Geneticist Constantly Signs out Cases

New Variant Assessments and Knowledge Base Updates

Cases / Identified Variants

GenelInsight
- Report Generation Engine
- Knowledgebase

GenelInsight Continuously Grows

Reports

Treating Clinician Consumes Reports

Occurs Automatically on Knowledgebase Update
No Case Level Work Required
### GeneInsight Clinic® | Surfacing Alerts

<table>
<thead>
<tr>
<th>Report Identifier</th>
<th>Report Status</th>
<th>Test</th>
<th>Overall Interpretation</th>
<th>Indication</th>
<th>Specimen</th>
<th>Genomic Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab-B Demo 0009 (LAB-HERO-B)</td>
<td>FINAL</td>
<td>03/26/2013 11:35 AM</td>
<td>Pan Cardiomyopathy Panel (51 Genes)</td>
<td>(Possibly Cleared)</td>
<td>Clinical diagnosis of HCM</td>
<td>No specimen recorded</td>
</tr>
<tr>
<td>Mouse, Minnie 0009 (PHS-EMR) 02/02/1992 (21)</td>
<td>Variant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Current Category**

Pathogenic (03/26/2013)

**Report Category**

Unknown Significance
HCM Variant Example
MYBPC3 c.927-9G>A

Novel Variant Detected in LMM Patient

3rd Affected Patient with Variant Identified

GeneInsight Clinic Launches at Partners

Functional Studies Demonstrate Variant is Pathogenic

New Cases:

VUS Likely Pathogenic Pathogenic

Alerts triggered to clinicians tracking patients through GeneInsight Clinic
Partners HealthCare Contributors to GeneInsight and Enterprise Genetic IT Strategy

Executive Leadership
Peter Markell
Anne Klibanski
Scott Weiss
David Louis
Jeff Golden
Brent Henry

Partners Innovation
Chris Coburn
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Trung Do (GeneInsight President)
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Chet Graham
Lei Lei Hien
Robert Hurley
Carly Mailly
Terry O'Neill
Mike Oates
Frank Russell
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Fei Wang

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Birgit Funke
Matt Lebo
Sami Amr
Heather McLaughlin
Heather Mason-Suares
Beth Duffy
Lisa Mahanta
Missie Kelly
Amy Lovelette-Hernandez
Mitch Dillon
Andrea Muirhead

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Kim Durniak

RISC
Shawn Murphy
Natalie Boutin
Chris Herrick
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PPM
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Meini Sumbada Shin
Robert Green
Natalie Boutin

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Steve Flammini
John Pappas
Beth King
Pat Rubalcaba
Michael Muriph
Michael Sperling
Roberto Rocha

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Hong Lou
Steve Raymond
Mike Whiteman

Information Security
Joe Zurba
Tim Trow
Jason Marchant
Brian Mertens
Dan Fitzpatrick

IRB
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Libby Hohmann
Judy Scheer

BWH Cardiology
Calum Macrae
Kricket Seidman

BWH Pulmonary
Benjamin Raby

MGH Genetics
David Sweetser

ERIS
Brent Richter
Allan Harris
Fabio Martins
Aaron Zschau
The GeneInsight Network

GeneInsight Lab
- Reporting Engine
- Genomic Knowledgebase
- Case Repository

GeneInsight Clinic
- Patient Genomic Profile Repository
- Alerting Engine
- EHR Connectivity
Optimal Diagnosis Involves Lots of Heterogeneous Data

Fully Personalized Medicine Would Involve Leveraging All Potentially Useful Data To Continuously Improve Diagnostic Capabilities
Generating and Applying Across Data Types

Diagram:

- Diagnosis
  - Clinical Chemistry
  - Imaging
  - Anatomic Pathology
  - Patient Exams
  - Genetics and Other Omics
  - Department Specific Testing

Continuous Learning Engines
Thank You!