Biomedical Informatics, Transforming Healthcare one individual at a time

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Source: Interview with Bill Nelson, CEO, Intermountain Healthcare

Key Determinants of one’s health

- Genetics: 30%
- Behavior: 40%
- Public Health: 20%
- System: 10%
Healthcare has always been an information business, but never to this extent

- Availability of Health data under individual control
- Inexpensive Genotype & Phenotype data
- Next Generation Gene Sequencing and bioinformatics tools
- Availability to combine health and environment data
- Personalized Therapies
Evolution of Health Record Architectures
Evolution of Health Record Architectures
Why the individual Model?

The history behind the PCHR model of HCIT

- Developed to solve the interoperability issues in the US healthcare system, where business models encourage a lack of interoperability
- It has benefits outside of the US system, it transfers risks to third party and solves the privacy and authentication issue once
- Platform function allows for an App Store style ecosystem to develop
- Replaces a very complex IT problem with a much simpler one
What does a PCHR look like?
Oh, to be in England

National database of NHS medical records to be dismantled under Tory plans

The national database of NHS medical records would be dismantled under Tory plans which could see records available online with Google or Microsoft.
Public Health Applications
Looking to the future of PCHR, beyond data

- Need for consumer utility, small wins
- Higher rates of Compliance to treatment regiments
- Enable new tools in public health
- Radically transform the economics of clinical research
- Accelerate the pace of pharmacovigilance
- Allow direct participation in medical discoveries to the individual
Rates of discovery are accelerating
Why is the pace of discovery accelerating?

Projected output of 1000 Genomes Project
JGI + 1000 Genomes actuals (Nov12)
Second generation technologies begin

Historic doubling rate: 14.35 months

one human genome: ~3 billion base pairs

Transistors per microprocessor
Nucleotide base pairs per day
Nucleotide base pairs per dollar

02 Dec 2008

02 Dec 2008
The Promise of Genetic Testing

Today, more than 500 genetic tests can help answer many important medical questions:

Could I have breast cancer?

Should I have a mastectomy?

Could I have ovarian cancer?

Coumadin? Warfarin?

I am worried about grandpa taking a blood thinner.

What does all of this mean???
Matter of Translation
(a personal story of humiliation)
**PPARγ Pro12Ala and diabetes**

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**Estimated risk (Ala allele)**

- Oh et al.
- Deeb et al.
- Mancini et al.
- Clement et al.
- Hegele et al.
- Hasstedt et al.
- Lei et al.
- Ringel et al.
- Hara et al.
- Meirhaeghe et al.
- Douglas et al.
- Altshuler et al.
- Mori et al.
- All studies

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**Overall** $P$ value = $2 \times 10^{-7}$

**Odds ratio** = 0.79 (0.72-0.86)

Ala is protective

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**Sample size**

**Courtesy J. Hirschhorn**
Costs of typical Gene Research
i2b2 Hive: A Translational Toolkit

Adoption 21+ AMC’s
Commercial and academic development efforts
Free and open source

https://www.i2b2.org/software/
New paradigms in Genomics research
Problems with current approach in Genomic Research

• Focus on monogenetic diseases (i.e., just a few diseases)
• Does not leverage new biomedical informatics and genomic technologies
• "Excludes patients from immediate benefit"
  • One-way interaction with participants
  • Knowledge not communicated back to patients in timely fashion
  • Patients are not partners in the research enterprise
• Discovery cycle is slowed
• Utilizes few patients and for a limited time
Gene Partnership Program Approach

• Radically transform the economics of research
• Accelerate the pace of discovery and cure
• Focus on polygenic diseases (i.e., most diseases)
• Leverage leading edge biomedical informatics and genomics technologies
• Reestablish the link between researchers and research subjects, using the “informed cohort” model

Engage every patient in the research enterprise, empowering them with cutting edge tools from biomedical informatics and genomics
Decoding genetic–environmental interactions is the next step.

Current research protocols
Effective for those rare diseases caused by a single gene defect (monogenic).

Monogenic or multigenic

… Decoding genetic–environmental interactions is the next step.

Most diseases caused when multiple genes (multigenic) interact with multiple triggering factors.
Small number of patients over limited duration studies

- Researchers able to get some data on some of their patients
  - Data is siloed and difficult to share
  - Patient population is too small to correlate genetic data with risk factors
In traditional medical studies concerns over privacy has broken the doctor-patient link, disallowing subsequent communication. As a result, participants are passive and can’t be informed of medically relevant findings. GPP employs a collaborative clinical research regime, the Informed Cohort (IC), establishing a true partnership with patients.

- Participants and their families are actively engaged; participants can:
  - receive timely notice of beneficial discoveries – tailored and targeted information relevant to their disease
  - control level of involvement and communication
- Added benefits increase willingness of patients to join the study

New Paradigm in Research
The GPP Process
Patient meets with a genetic counselor, decides to enroll

Patients provide blood or saliva specimens for genetic analysis, and clinical information

Genomic and clinical information is stored in the patients’ PCHR
  – Germane study data are stored in an anonymized research database

When discoveries or important clinical information becomes available, Children’s Hospital can communicate privately and anonymously to patients through the PCHR
  – Informed Cohort Oversight Board provides ethical oversight

Patients are linked to clinical care and research with a PCHR
Children as the perfect cohort

Why Kids?
Studying childhood diseases presents a unique opportunity to:
– Clearly identify phenotypic manifestations of genetic traits
– *Before* environmental impacts overwhelm

Many adult diseases have highly predictive childhood antecedents
The Ultimate Prize

Personalized Medicine
A matter of economics

Apply a **chronic disease-centric approach** to public health burdens: cardiovascular disease, cancers, neurological disease, metabolic disorders, and pediatrics.

Use molecular scanning technologies to identify at-risk individuals prior to disease symptoms, and to **develop and test therapies** (with companion diagnostics, as feasible).

Partner with researchers, clinicians, and companies to accelerate the **translation of new discoveries into product development and then clinical practice**, to prevent or mitigate the onset of disease.

Apply the latest therapies, through an integrated health system, to benefit patients and **speed availability of new, targeted therapies**.

Integrate **health information technology** to enable broad-based clinical decision support for individualized patient management.

Share knowledge that helps to **alleviate or delay the onset of chronic disease** and decrease the time individuals are sick at the end of life.
In ‘Boomer’ Diseases, such as Alzheimer’s, Impact and Costs Will Escalate Dramatically Without New Interventions

Example: Alzheimer’s

Current Drug Discovery Methodology

Average cost: USD 230 million
Time to market: 14.8 Years

Starting point is about
10,000 compounds
1000 in vitro trial
20 in vivo trial
10 human clinical trials

Genomics information is suppose to be the short cut in this process
Millennium Pharmaceuticals was a case in point, it did not quite work that well
identify genes that classify the population into “high” and “low” risk
built a broad-based genetic testing infrastructure to classify individuals using repositories of PCHR
incorporate pointers to recruit “high” risk individuals into clinical trial
run a series of small trials drawing to develop primary prevention drugs for AD in the next decade
educate the authorities (such as FDA in the US) that targets are robust enough for approval of drugs without a 30 year prospective trial where we lose a generation in the process
Embed the genome into the HER/PCHR
Allow HIPAA-compliant messaging and interventional distributed trials
Secure and authenticate transactions and data flow
Link clinical information system with a research database that can connect to other HIT systems
Build a flexible clinical decision support module that allows physicians to understand molecularly-guided strategies
Enable a “learning” CDS that constantly refines itself with the data flows to optimize clinical care
I2b2- Informatics from Biology to the Bedside
https://www.i2b2.org/
Children Hospital Boston Informatics Program
http://chip.org/
Ignite Institute for Personalized Health
http://www.ignitehealth.org/

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