Biomedical Informatics, Transforming Healthcare one individual at a time

NIA 2009
Canberra, Australia

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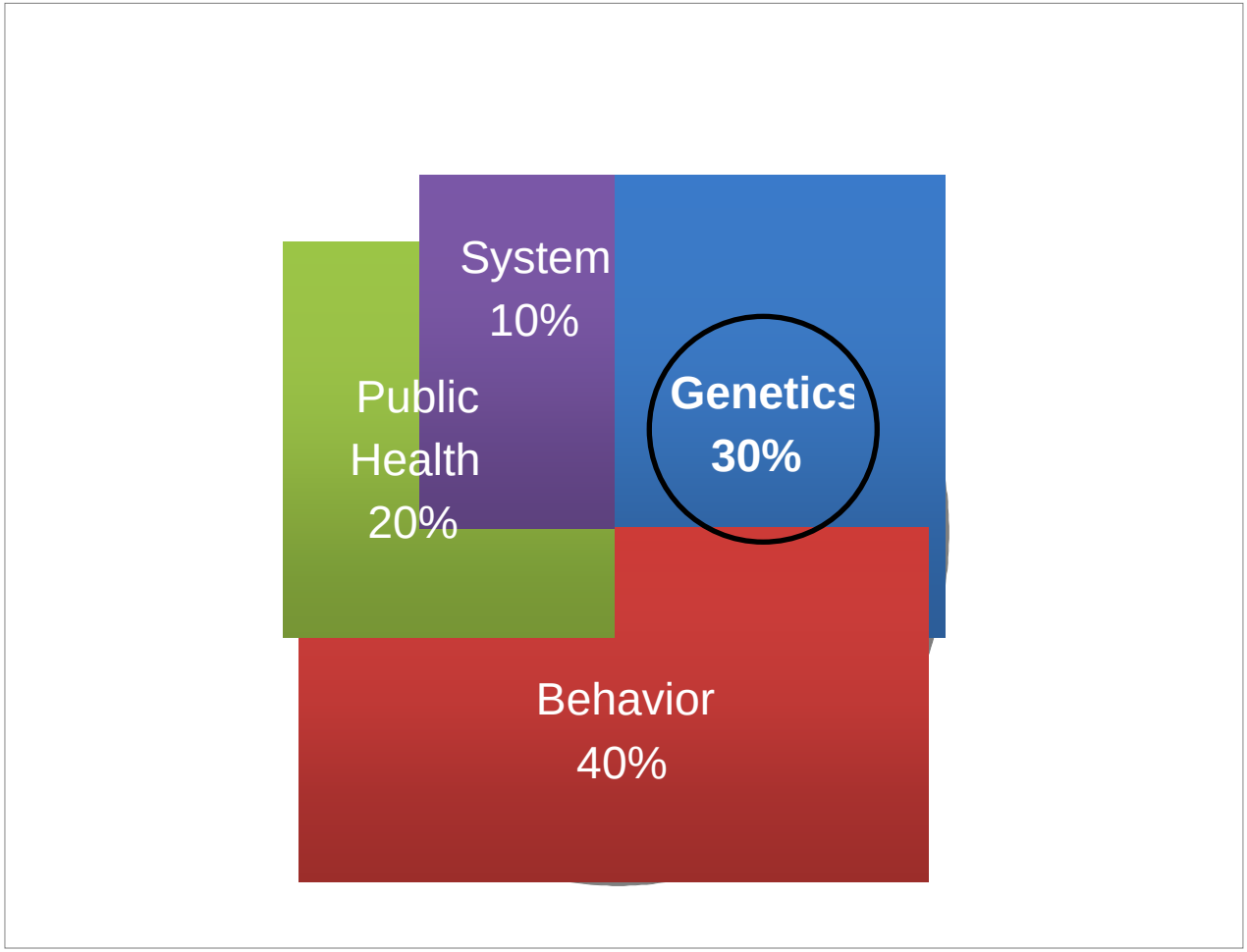
Center for Biomedical Informatics

Key Determinants of one's health



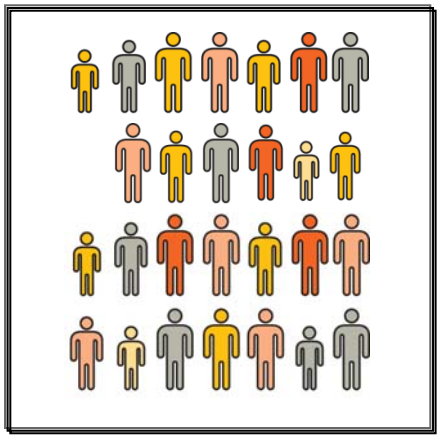
Source: Interview with Bill Nelson, CEO, Intermountain Healthcare

Themes

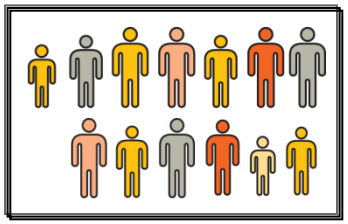
Healthcare has always been an information business, but never to this extent

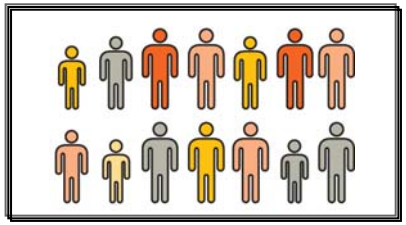
- Availability of Health data under individual control
- Inexpensive Genotype &Phenotype data
- Next Generation Gene Sequencing and bio informatics tools
- Availability to combine health and environment data
- Personalized Therapies

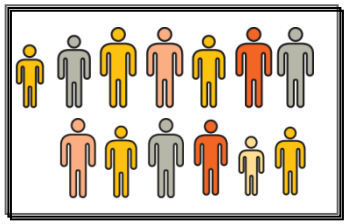
Evolution of Health Record Architectures



Stalinist

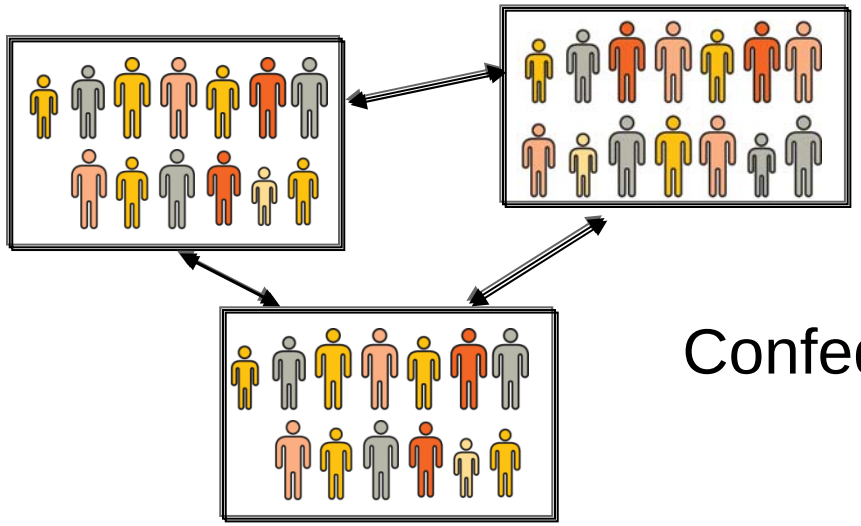




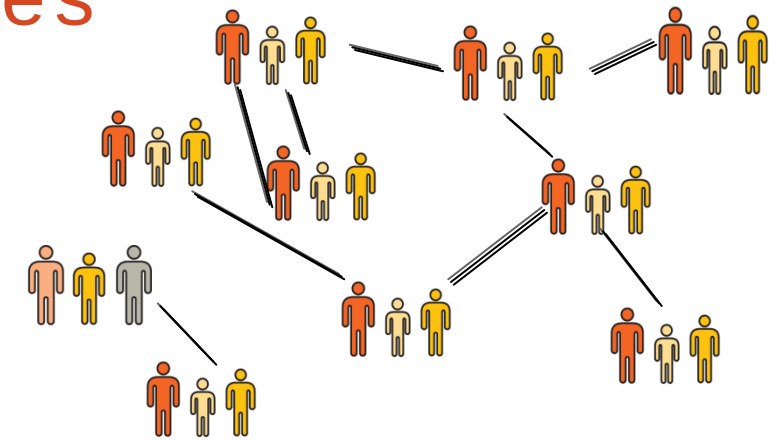


Feudal

Evolution of Health Record Architectures



Confederate



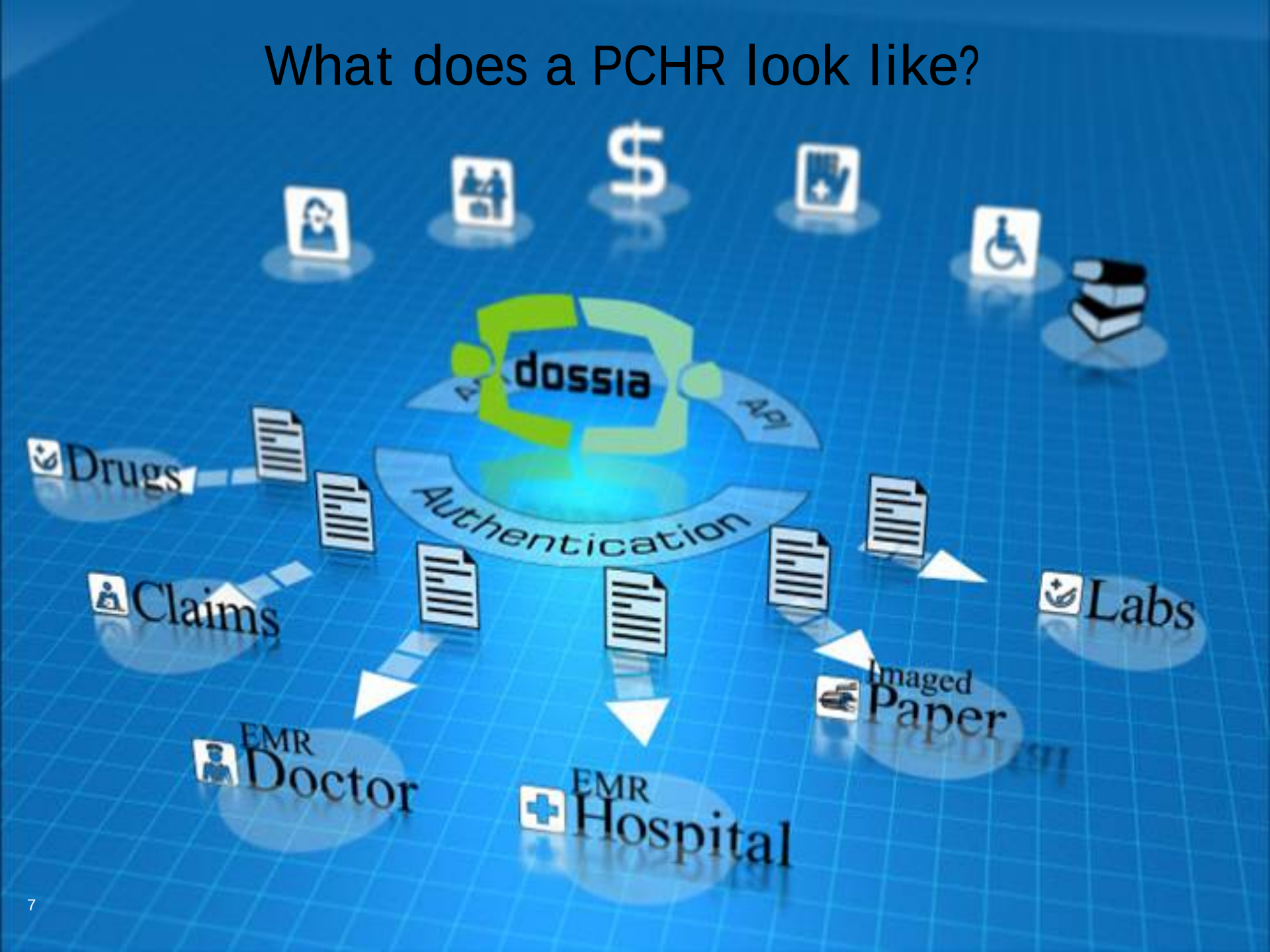
Individual

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?



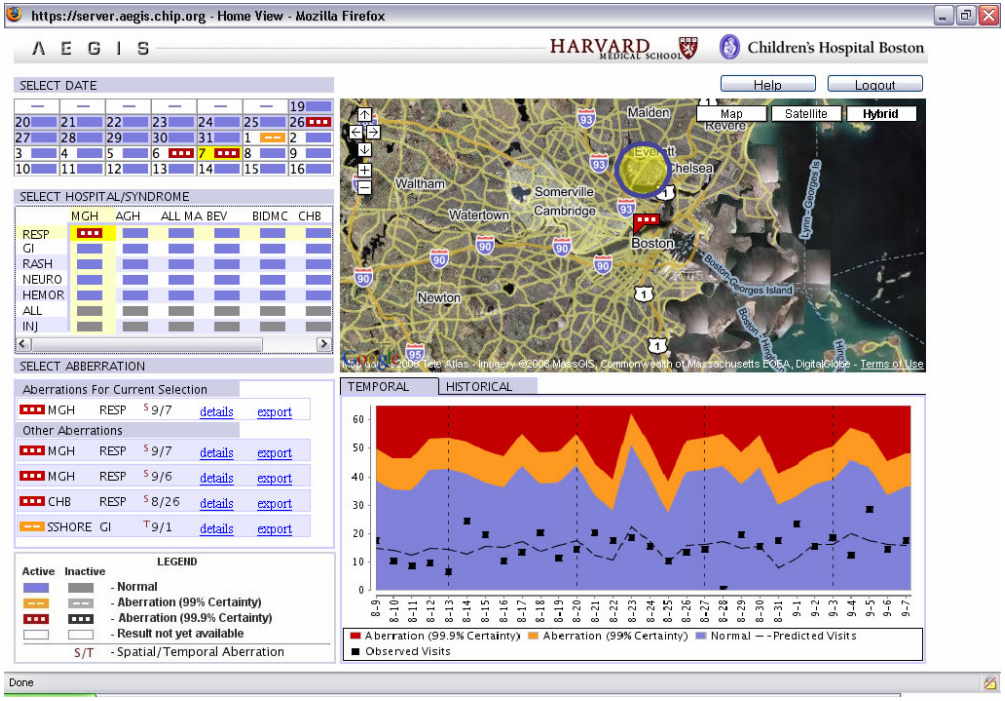
Oh, to be in England

Telegraph.co.uk

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

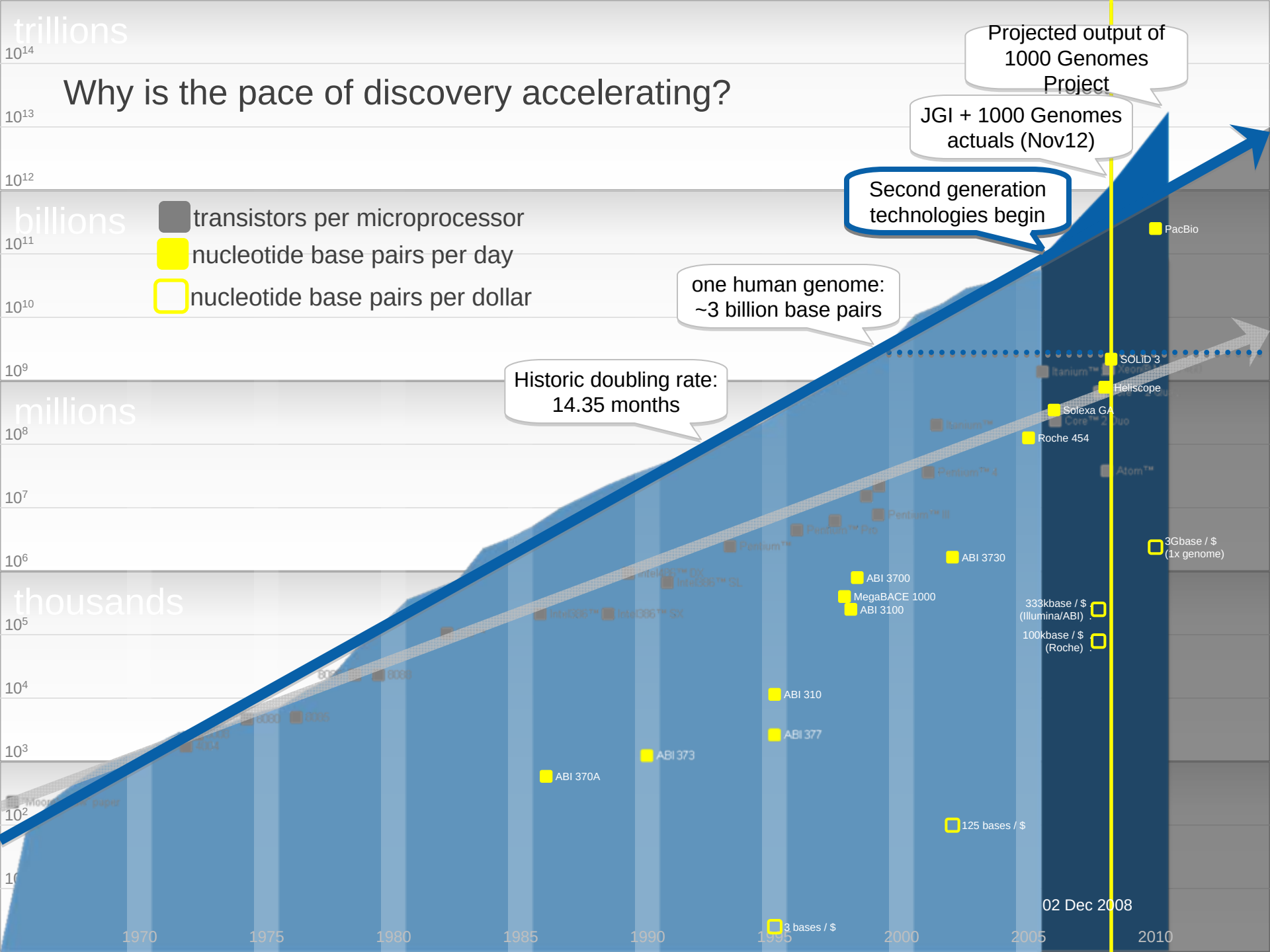


HealthMap
Global Disease Alert Map

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


trillions
billions
millions
thousands
10^{14}
10^{13}
10^{12}
10^{11}
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
10^{4}
10^{3}
10^{2}
Why is the pace of discovery accelerating?
transistors per microprocessor
nucleotide base pairs per day
nucleotide base pairs per dollar
Projected output of 1000 Genomes Project
JGI + 1000 Genomes actuals (Nov12)
Second generation technologies begin
one human genome: ~3 billion base pairs
Historic doubling rate: 14.35 months
PacBio
SOLID 3
Heliscope
Solexa GA
Roche 454
ABI 3730
3Gbase / $ (1x genome)
ABI 3700
MegaBACE 1000
ABI 3100
333kbase / $ (Illumina/ABI)
100kbase / $ (Roche)
ABI 310
ABI 377
ABI 373
ABI 370A
125 bases / $
3 bases / $
02 Dec 2008
1970
1975
1980
1985
1990
1995
2000
2005
2010

The P

What does all of this mean???

n help

ions

cer?

BrCA1

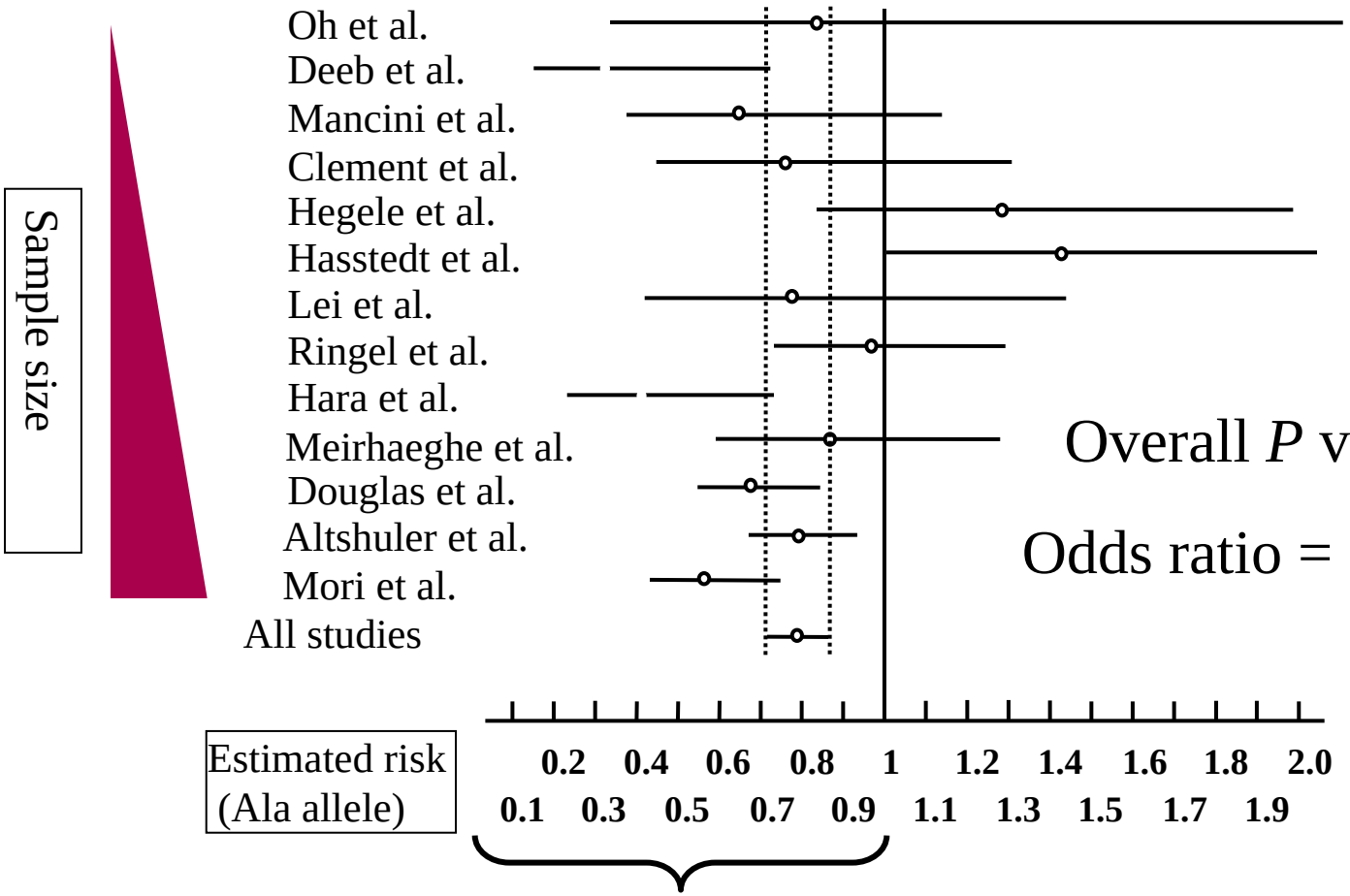
VKORC1

CYP2C9 1 OR 2

Matter of Translation

(a personal story of humiliation)

PPARγ Pro12Ala and diabetes

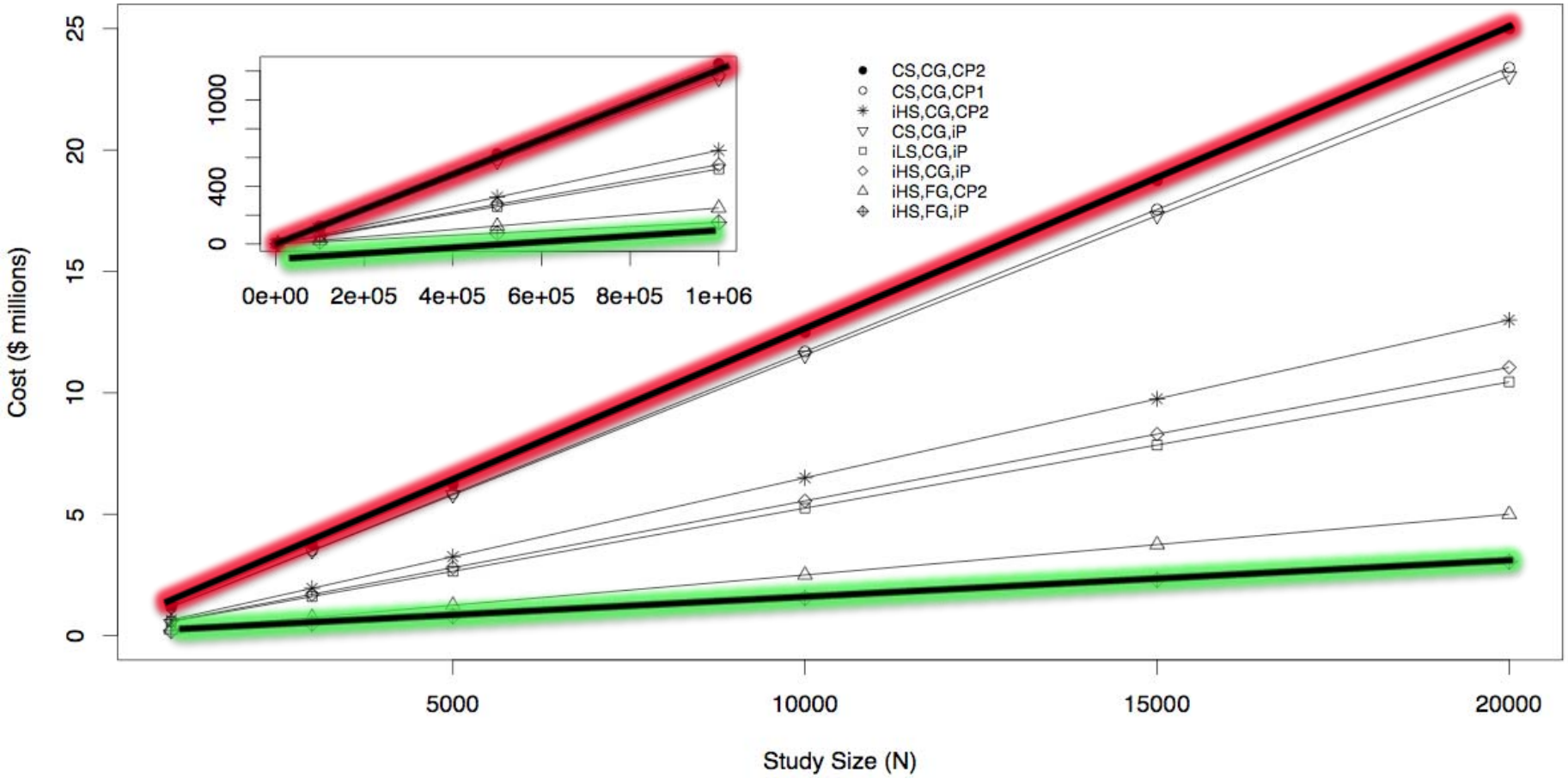


Overall *P* value = 2×10^{-7}

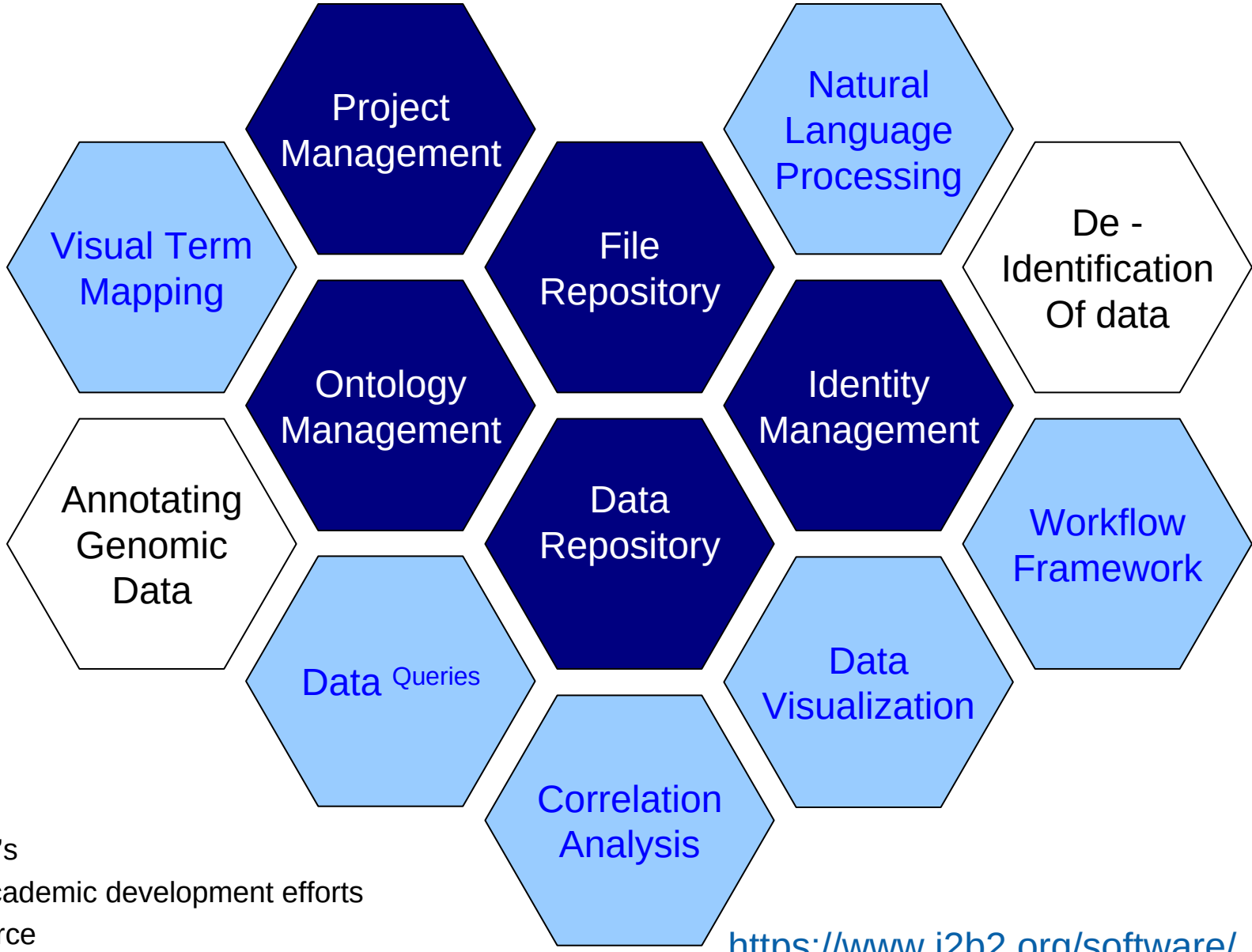
Odds ratio = 0.79 (0.72-0.86)

Courtesy J. Hirschhorn

Costs of typical Gene Research



i2b2 Hive: A Translational Toolkit



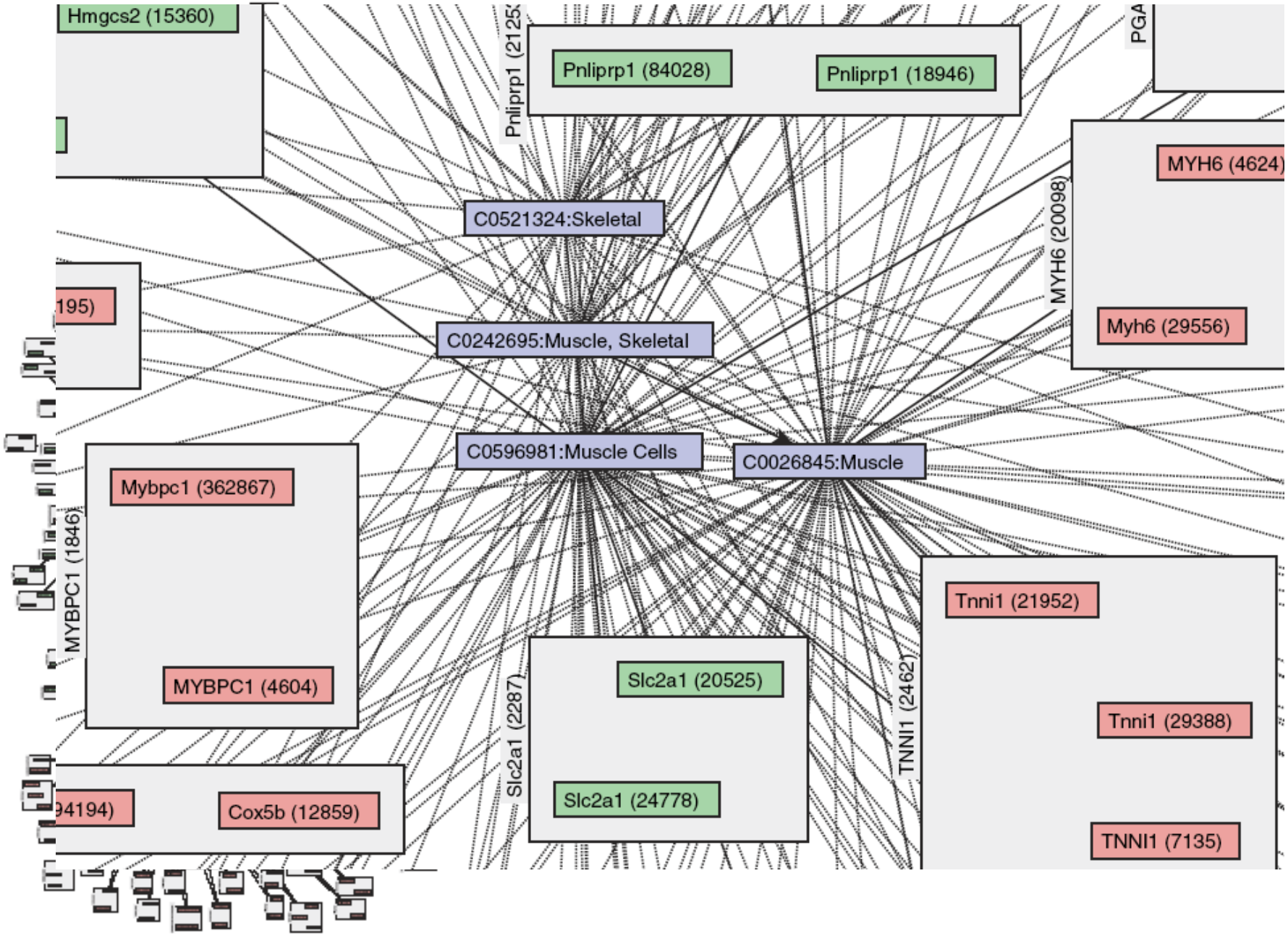
Adoption 21+ AMC's

Commercial and academic development efforts

Free and open source

https://www.i2b2.org/software/

a


Hmgcs2 (15360)
Pnliprp1 (84028)
Pnliprp1 (18946)
C0521324:Skeletal
MYH6 (4624)
MYH6 (20098)
Myh6 (29556)
C0242695:Muscle, Skeletal
C0596981:Muscle Cells
C0026845:Muscle
Mybpc1 (362867)
MYBPC1 (1846)
MYBPC1 (4604)
Tnni1 (21952)
Slc2a1 (20525)
Slc2a1 (2287)
Tnni1 (29388)
TNNI1 (2462)
Slc2a1 (24778)
Cox5b (12859)
TNNI1 (7135)

New paradigms in Genomics research

Problems with current approach In Genomic Research

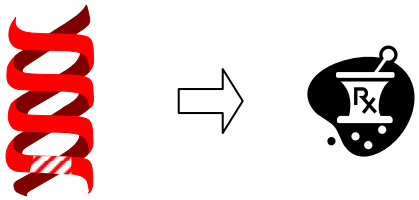
- Focus on monogenic diseases (i.e., just a few diseases)
- Does not leverage new biomedical informatics and genomic technologies
- **Excludes patients from immediate benefit**
  - One-way interaction with participants
  - Knowledge not communicated back to patients in timely fashion
  - Patients are 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

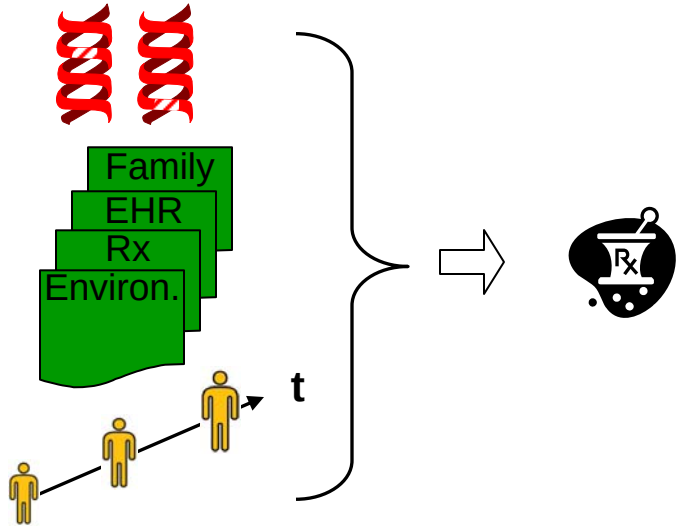
Current research protocols

Effective for those rare diseases caused by a *single gene* defect (monogenic)



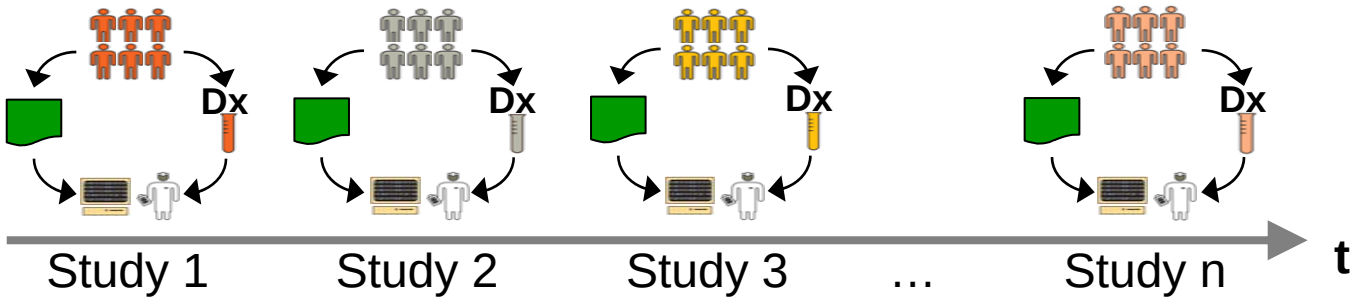
Monogenic or multigenic

… Decoding genetic–environmental interactions is the next step



Most diseases caused when *multiple genes* (multigenic) interact with multiple triggering factors

Current Research Model



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

New Paradigm in Research

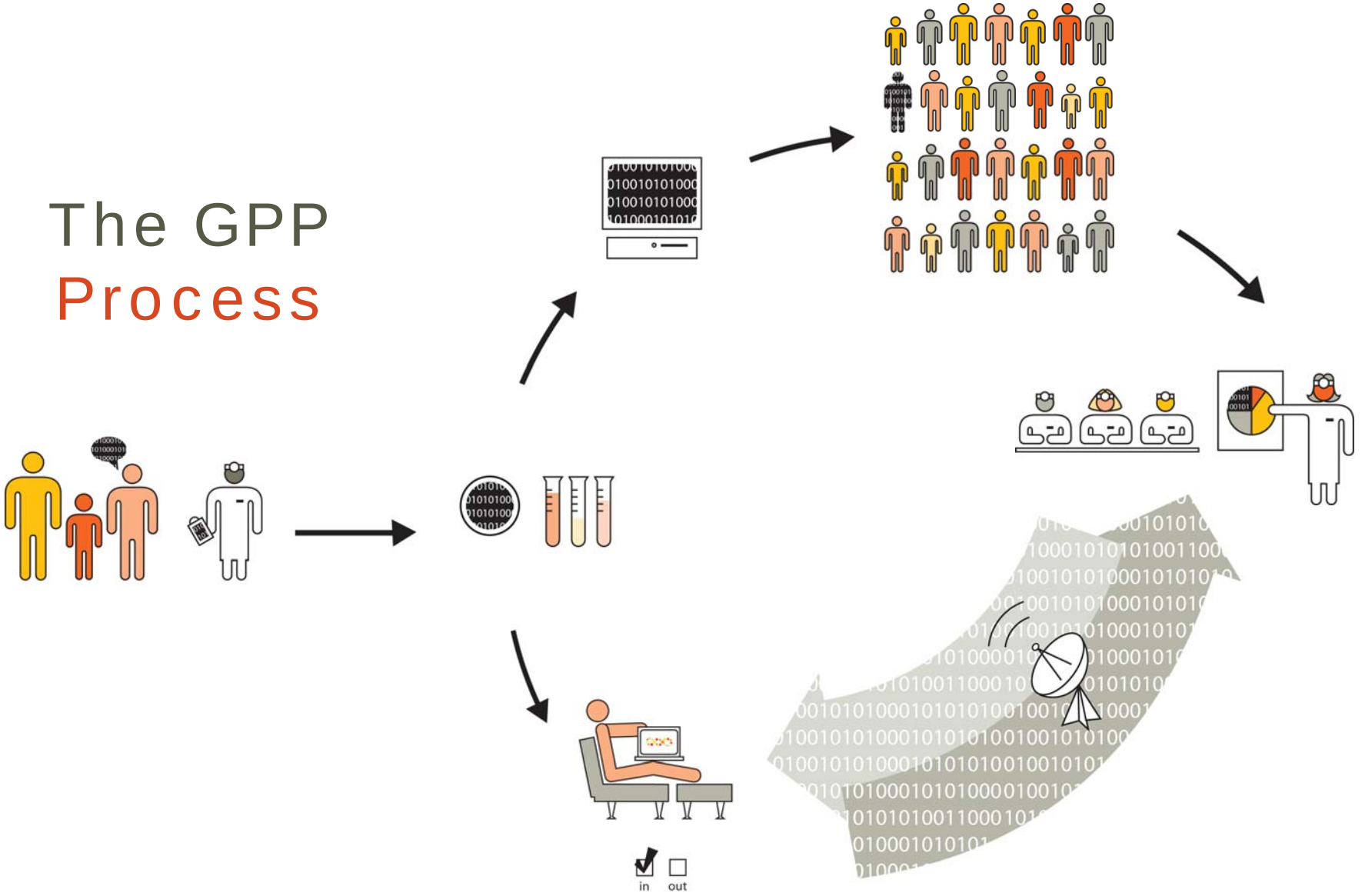
In traditional medical studies concerns over privacy has broken the doctor-patient link, disallowing subsequent communication

- 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

The GPP Process



The GPP Approach

- 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:

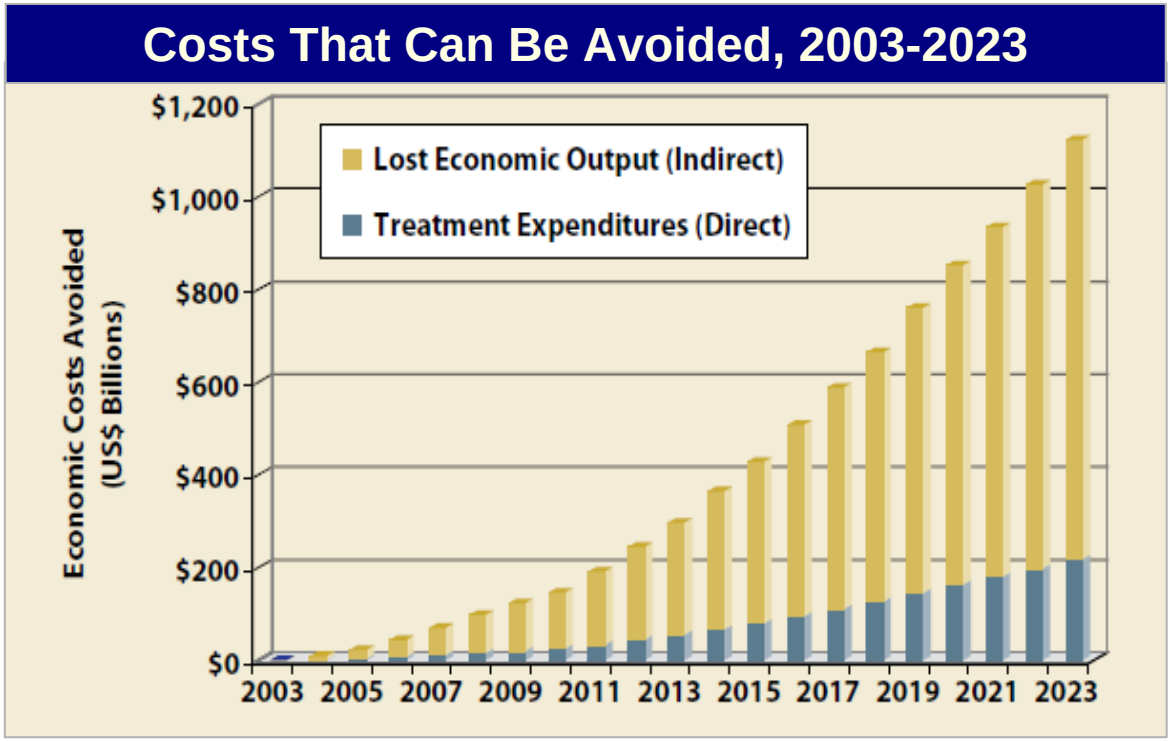
- Clearly identify phenotypic manifestations of genetic traits
- *Before* environmental impacts overwhelm

Many adult diseases have highly predictive childhood antecedents

The Ultimate Prize

Personalized Medicine

A matter of economics



Source: DeVol, R, Bedroussian, A, et al. An Unhealthy America: The Economic Burden of Chronic Disease. The Milken Institute. October 2007.

Personalized Medicine Strategy

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

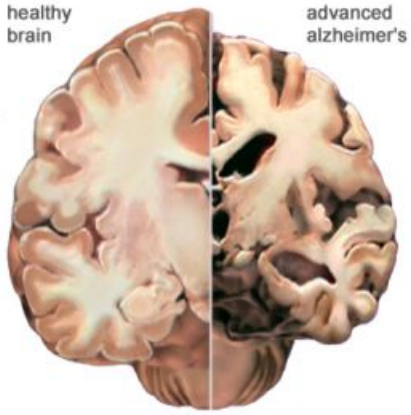
Use molecular scanning technologies to identify at-risk individuals prior to disease symptoms, and to **develop and test therapies** (with companion diagnostics, as feasible).

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.**

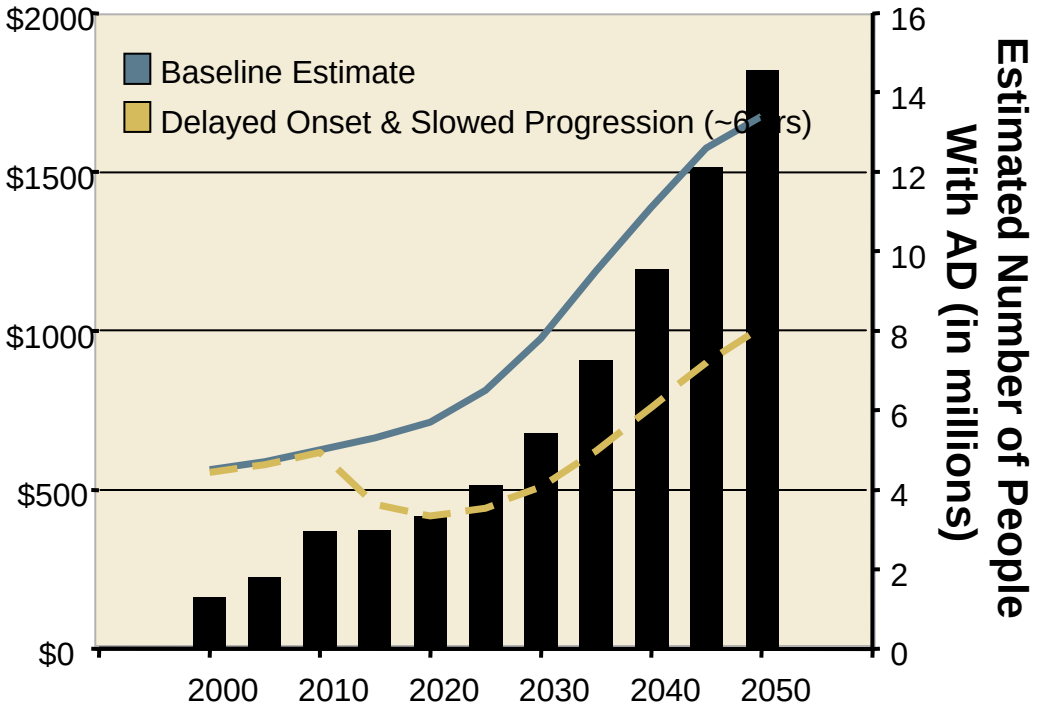
Integrate **health information technology** to enable broad-based clinical decision support for individualized patient management.

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.



Example: Alzheimer's

In 'Boomer' Diseases, such as Alzheimer's, Impact and Costs Will Escalate Dramatically Without New Interventions



Adapted from The Lewin Group Report, June 2004, "Saving Lives. Saving Money: Dividends for Americans Investing in Alzheimer Research, " The Alzheimer's Association (http://www.alz.org/Resources/FactSheets/Lewin_FullReport1.pdf)

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

New Process from end to end

- 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

Role of HCIT

- 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

Ignite Institute For Personal Medicine

More Information And Special Thanks

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/

Special thanks to:

- Isaac (Zak) Kohane,Harvard Medical School
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- George Margelis, Intel Australia
- Joan Edgecumbe, HISA