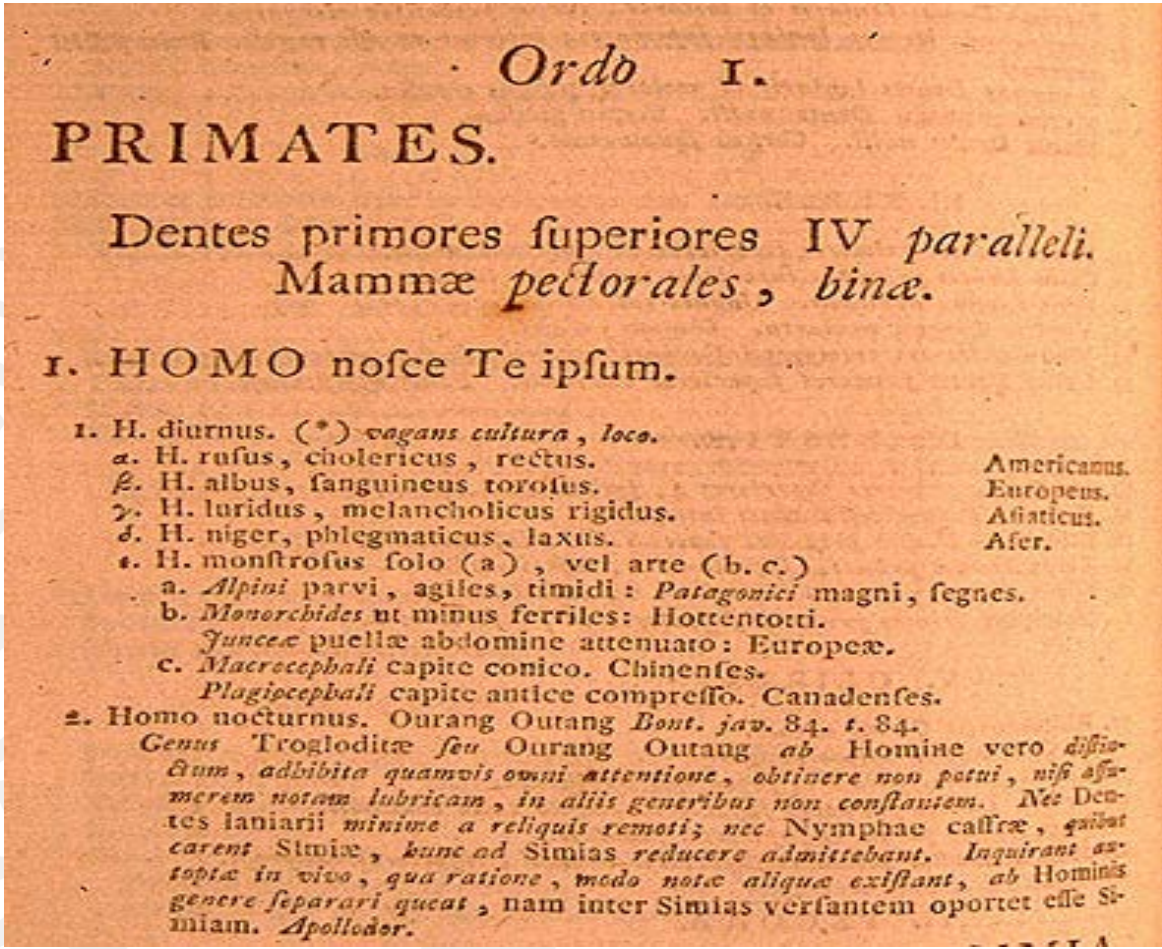
A Cautiously Optimistic View of the Future of Data-driven Genomically Informed Medicine

Isaac S. Kohane, MD, PhD

Overview

- Where we were
- Where we are heading now
- Where we could be.

Fundamental Medical Challenge: True Names of Disease



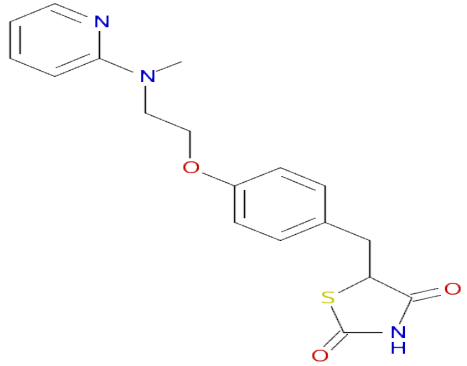
Ordo 1.

PRIMATES.

Dentes primores ſuperiores IV *paralleli.*
Mammæ *pectorales*, *binæ.*

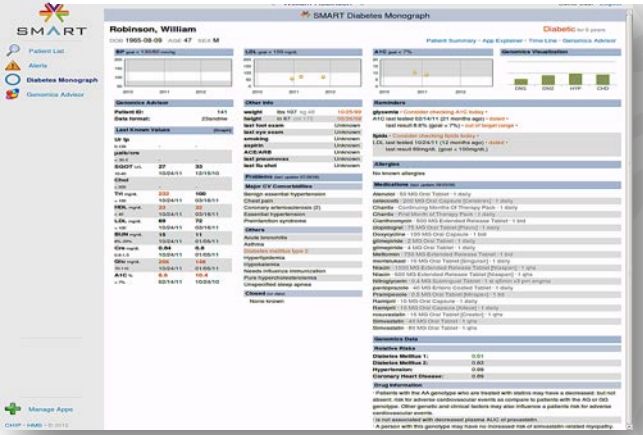
1. HOMO noſce Te ipſum.

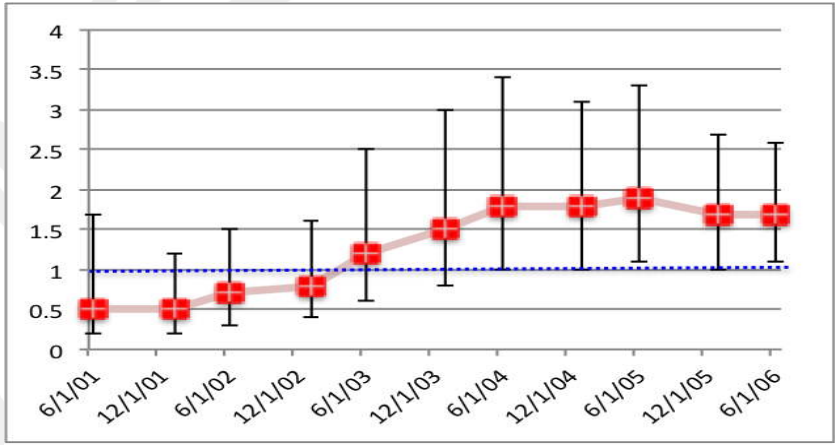
1. H. diurnus. (*) *vagans cultura, loco.*
   α. H. rufus, cholericus, rectus. — Americanus.
   β. H. albus, ſanguineus toroſus. — Europeus.
   γ. H. luridus, melancholicus rigidus. — Aſiaticus.
   δ. H. niger, phlegmaticus, laxus. — Afer.
   ε. H. monſtroſus ſolo (a), vel arte (b. c.)
   a. *Alpini* parvi, agiles, timidi: *Patagonici* magni, ſegnes.
   b. *Monorchides* ut minus ferriles: Hottentotti.
   Junceæ puellæ abdomine attenuato: Europeæ.
   c. *Macrocephali* capite conico. Chineſes.
   Plagiocephali capite antice compreſſo. Canadenſes.
2. Homo nocturnus. Ourang Outang *Bont. jav.* 84. *t.* 84.
   Genus Troglodytæ *ſeu* Ourang Outang *ab* Homine vero *diſſiciliùm, adhibita quamvis omni attentione, obtinere non potui, niſi aſſumerem notam lubricam, in aliis generibus non conſtantem. Nec* Dentes laniarii *minimè a reliquis remoti; nec* Nymphae caſſræ, *quibus carent* Simiæ, *hanc ad* Simias *reducere admittebant. Inquirant autoptæ in vivo, qua ratione, modo notæ aliquæ exiſtant, ab* Hominis *genere ſeparari queat*, nam inter Simias verſantem oportet eſſe Simiam. *Apollodor.*



i2b2

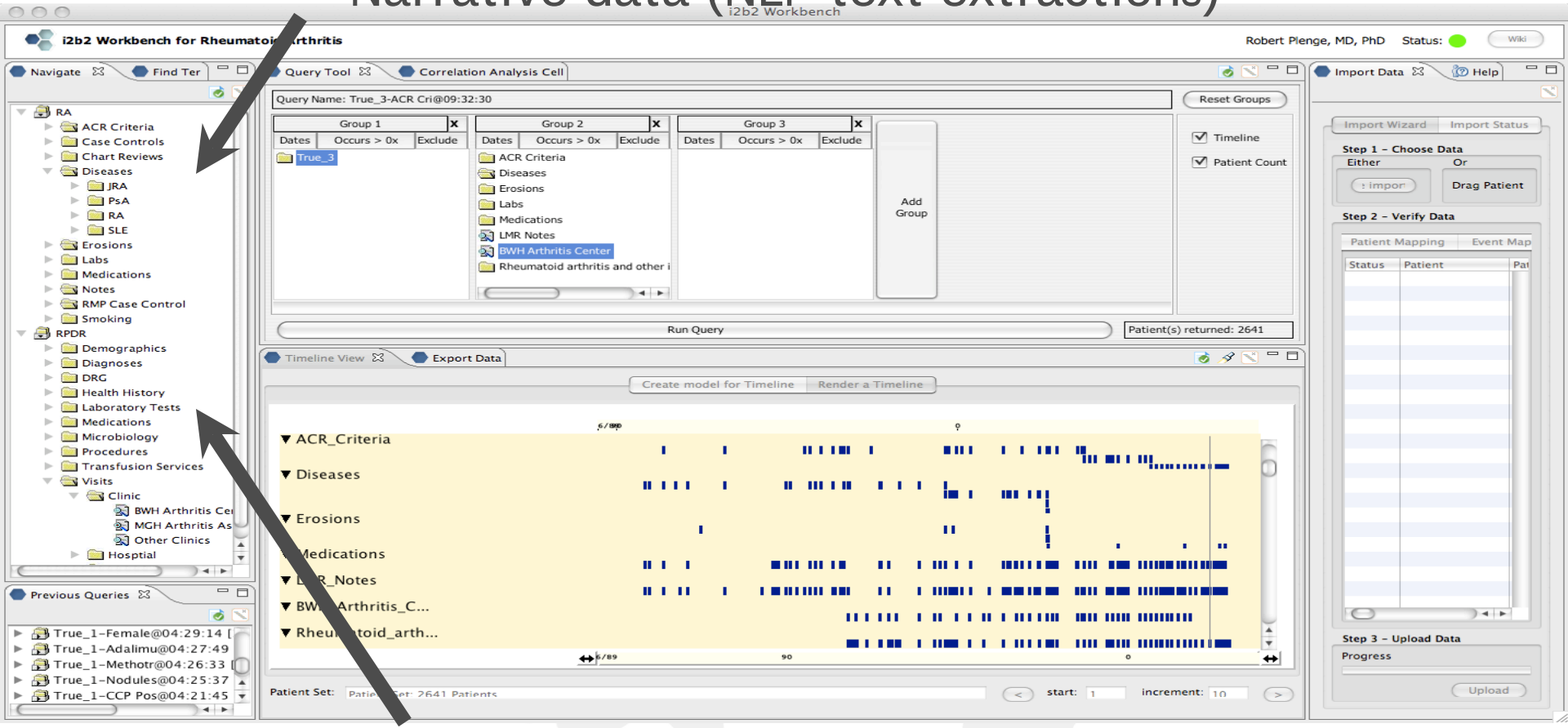
Informatics for Integrating Biology & the Bedside





SMART

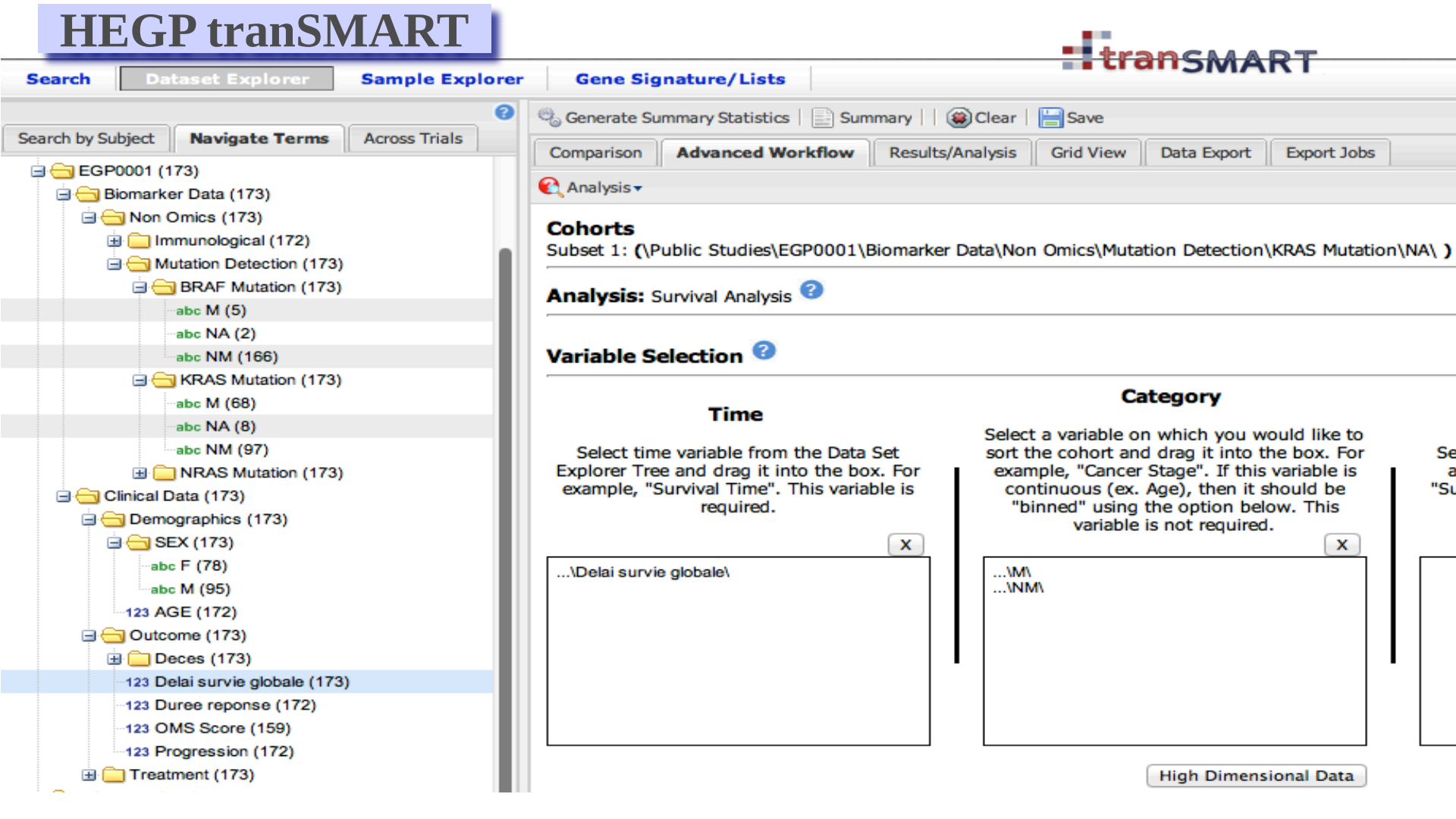
Narrative data (NLP text extractions)



Codified data (ICD9 codes, etc)

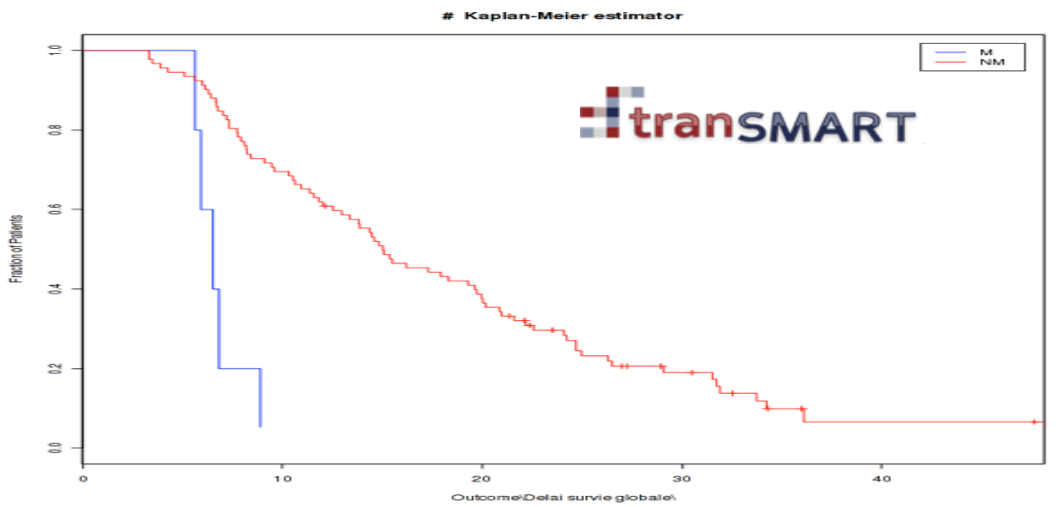
Odds Ratio
2.7
2.5
2.2
2.0
1.8
1.6
1.5
1.3
1.2
1.1
1.0
0.9
0.8
0.7
HLA
PTPN22
ANKRD55, IL6ST
PXK
TNFAIP3*
IRF5
CCL21*
CD40
STAT4
CTLA4
PRKCQ
RBPJ
IL2RA
C5ORF13
CD2,CD58
TRAF1, C5
CCR6
REL
SPRED2
CD28
BLK
AFF3
IL2, IL21
TNFAIP3
TAGAP
PRDM1
CCL21
KIF5A, PIP4K2C
IL2RB
SNP
GWAS
EHR EU ACPA+

HEGP tranSMART

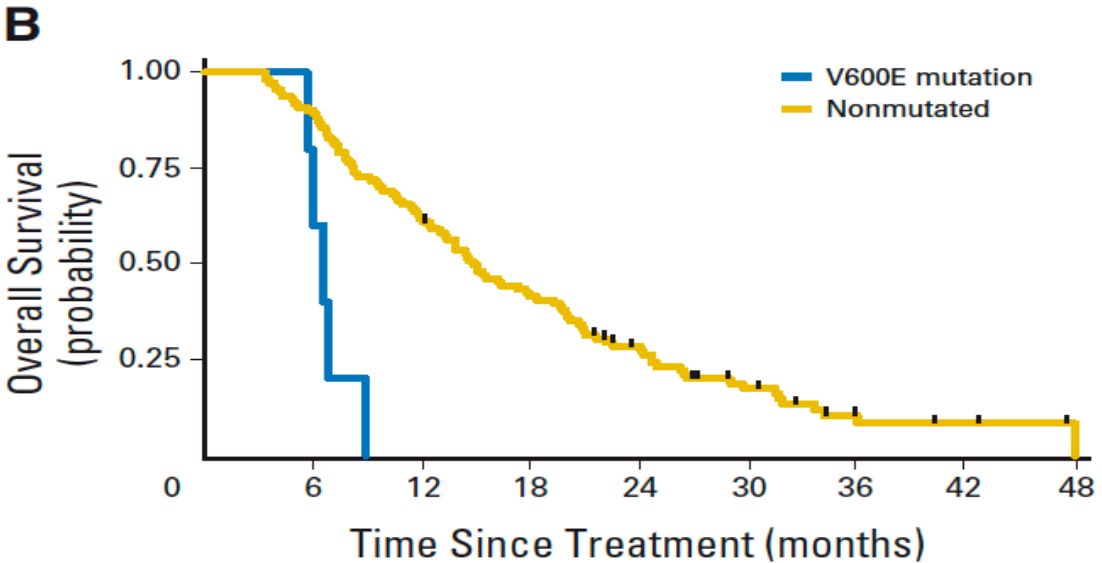


HEGP tranSMART

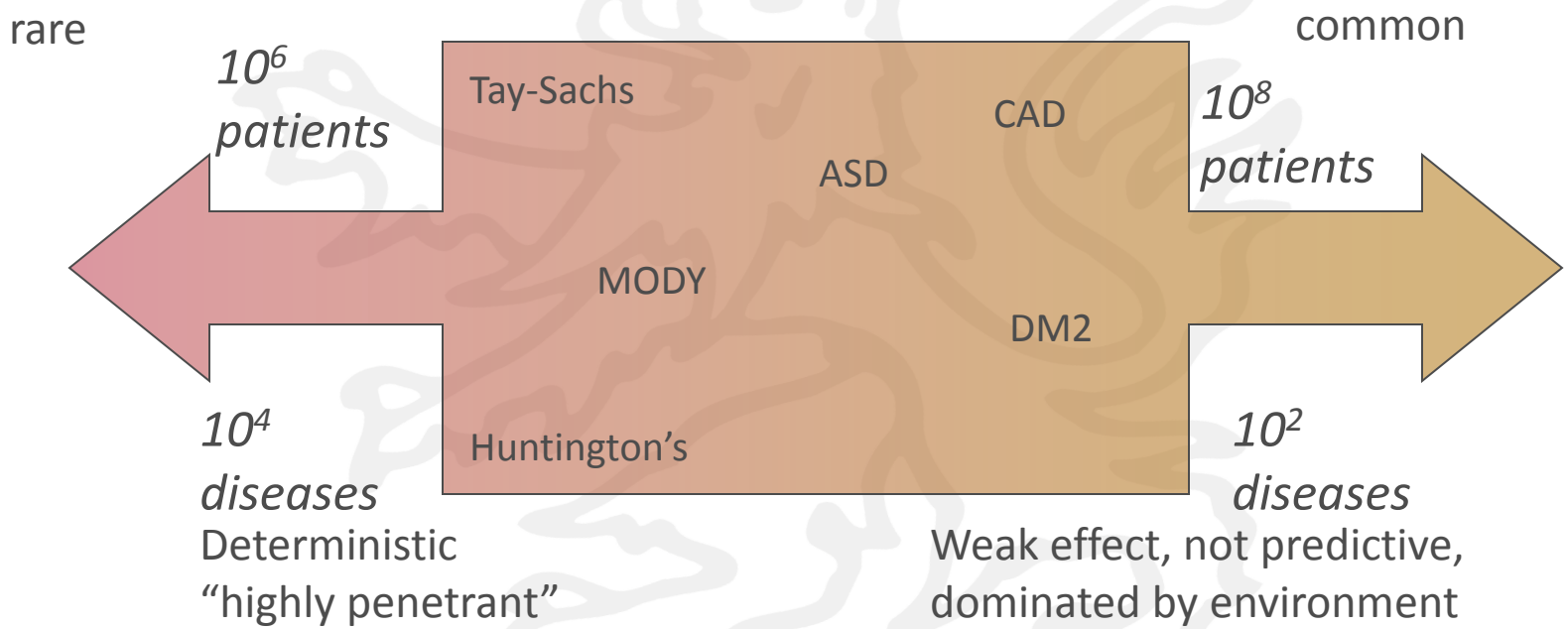
- R module in tranSMART



- Published figure in JCO



Common-Rare:Weak-Strong Spectrum

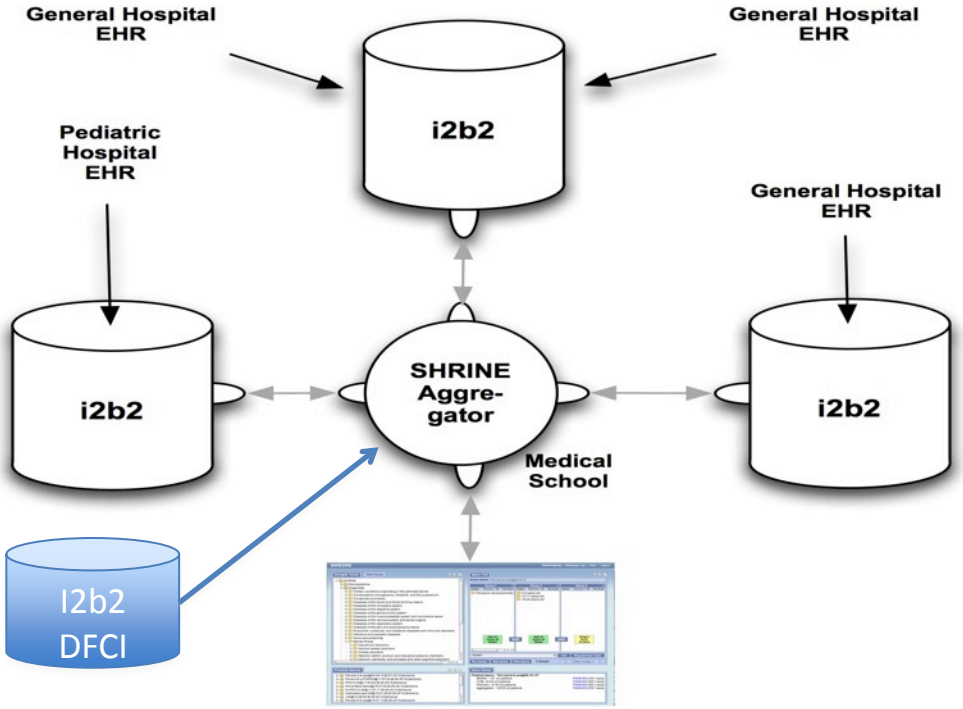


Rare &
COMMON

Needs BIG DATA

SHRINE: Governance over Technology

- Search routine clinical records from 5 major hospitals for:
  - Demographics
  - Diagnosis
  - Medications
  - Lab Results
- Reach N
  - Rare Dx
  - Small Effects
- 10 billion FACTS
- 6 million patients



Finding rare events of interest.

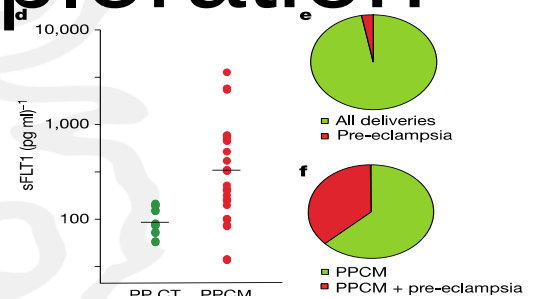
Cardiac angiogenic imbalance leads to peripartum cardiomyopathy

Ian S. Patten[1,2*], Sarosh Rana[3*], Sajid Shahul[4], Glenn C. Rowe[1], Cholsoon Jang[1], Laura Liu[1], Michele R. Hacker[3], Julie S. Rhee[3], John Mitchell[4], Feroze Mahmood[4], Philip Hess[4], Caitlin Farrell[1], Nicole Koulisis[1], Eliyahu V. Khankin[5], Suzanne D. Burke[5,8], Igor Tudorache[6], Johann Bauersachs[7], Federica del Monte[1], Denise Hilfiker-Kleiner[7], S. Ananth Karumanchi[5,8] & Zoltan Arany[1]

17 MAY 2012 | VOL 485 | NATURE | 333

samples from subjects with PPCM have been previously described[3]. Patients in both studies were predominantly Caucasian. Retrospective analyses of PPCM and pre-eclampsia in the Harvard teaching hospitals were performed using the Harvard Shared Health Research Information Network (SHRINE)[53], a de-identified repository of aggregate patient information.

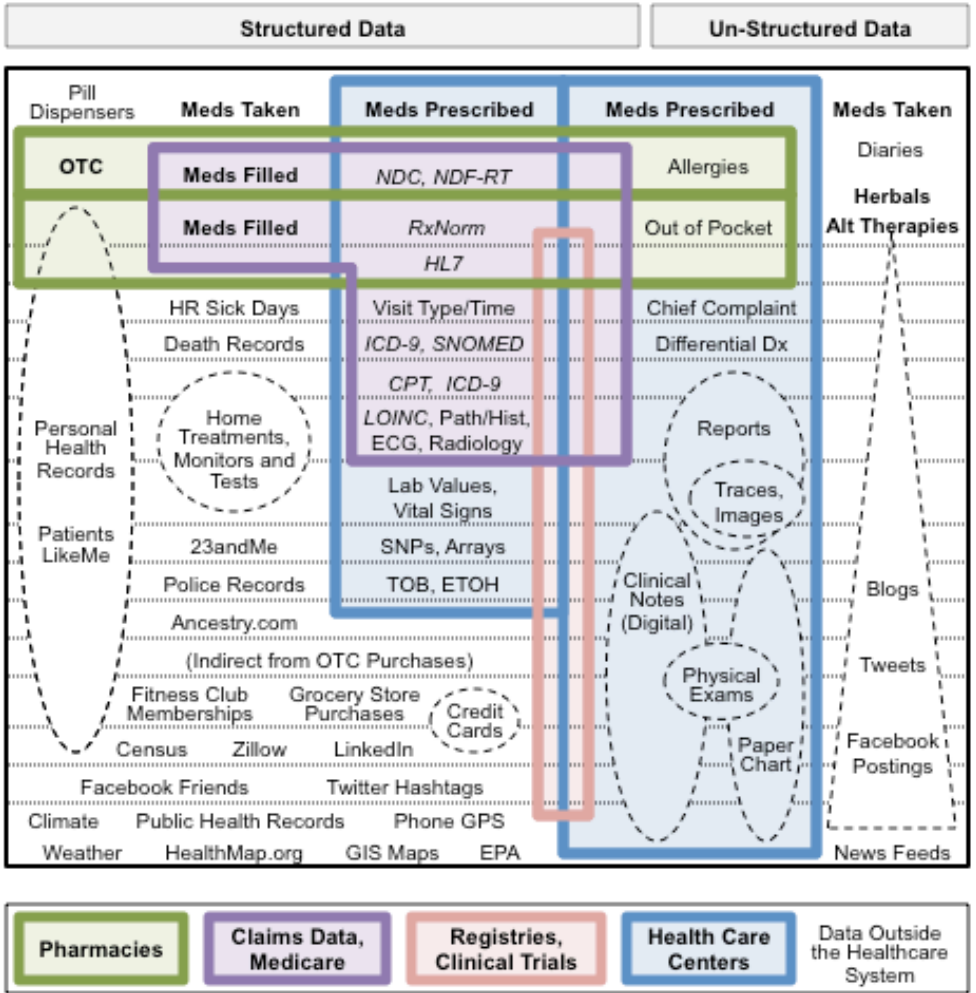
Importance of real-time exploration



Where is the missing information?

$$V_P = V_G + V_E + V_{GE}$$

"Big Data" Map of Patient Health



Courtesy
Griffin Weber

You are logged in as kobrien. Your Profile | Preferences | Log Out

HealthMap

Global health, local information

HealthMap for your SmartPhone More »

Search disease or location go Advanced Search Display Options:

Activity Index — Low / High — Country level — Province or local level

Vaccine preventable diseases | User Submitted Reports | H1N1 Swine Flu

440 Alerts Now Showing

Date: 24 Sep - 28 Sep | Diseases: all | Places: all | Sources: all | Categories: all

Source	Date	Summary	Disease	Location	Cases	Deaths	Significance	Stats
G	27 Sep	Klimovich: "The investigation proved the intentional poisoning ...	Poisoning	Togo			0 votes	
G	27 Sep	Epidemic outbreak of Lassa fever in Sierra Leone: Two ... - ...	Lassa Fever	Sierra Leone		2	1 vote	
G	27 Sep	Plague outbreak in China controlled - UPI.com	Plague	Nyingchi, Tibet, China			1 vote	

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Last update: 27 Sep 2010 04:00 | Next update: 27 Sep 2010 05:00

The NEW ENGLAND JOURNAL of MEDICINE

HealthMap
Global Disease Alert Map

Influenza A (H1N1) Reports

Source

- (•) Informal Sources (Media)
- ( ) Official Sources (ie: CDC, WHO)

All HealthMap Sources »

Category

- [ ] Ruled Out
- [x] Suspected Cases
- [x] Suspected Deaths
- [x] Confirmed Cases
- [x] Confirmed Deaths

Zoom to country

Mexico

La Jornada

Influenza A (H1N1) Virus, 2009 — Online Monitoring

John S. Brownstein, Ph.D., Clark C. Freifeld, B.S., and Lawrence C. Madoff, M.D.

Portada | Edición impresa | Especiales | Multimedia | Servicios | Escríbanos

Usted está aquí: Portada → 2009 → 04 → 01 → Veracruz: reporta agente municipal extraño brote epidémico que ha cobrado dos vidas

Veracruz: reporta agente municipal extraño brote epidémico que ha cobrado dos vidas

Enviar esta página a alguien
Imprimir esta página

La funcionaria de La Gloria informó que el raro padecimiento ha afectado a 60 por ciento de sus tres mil habitantes con infecciones respiratorias.

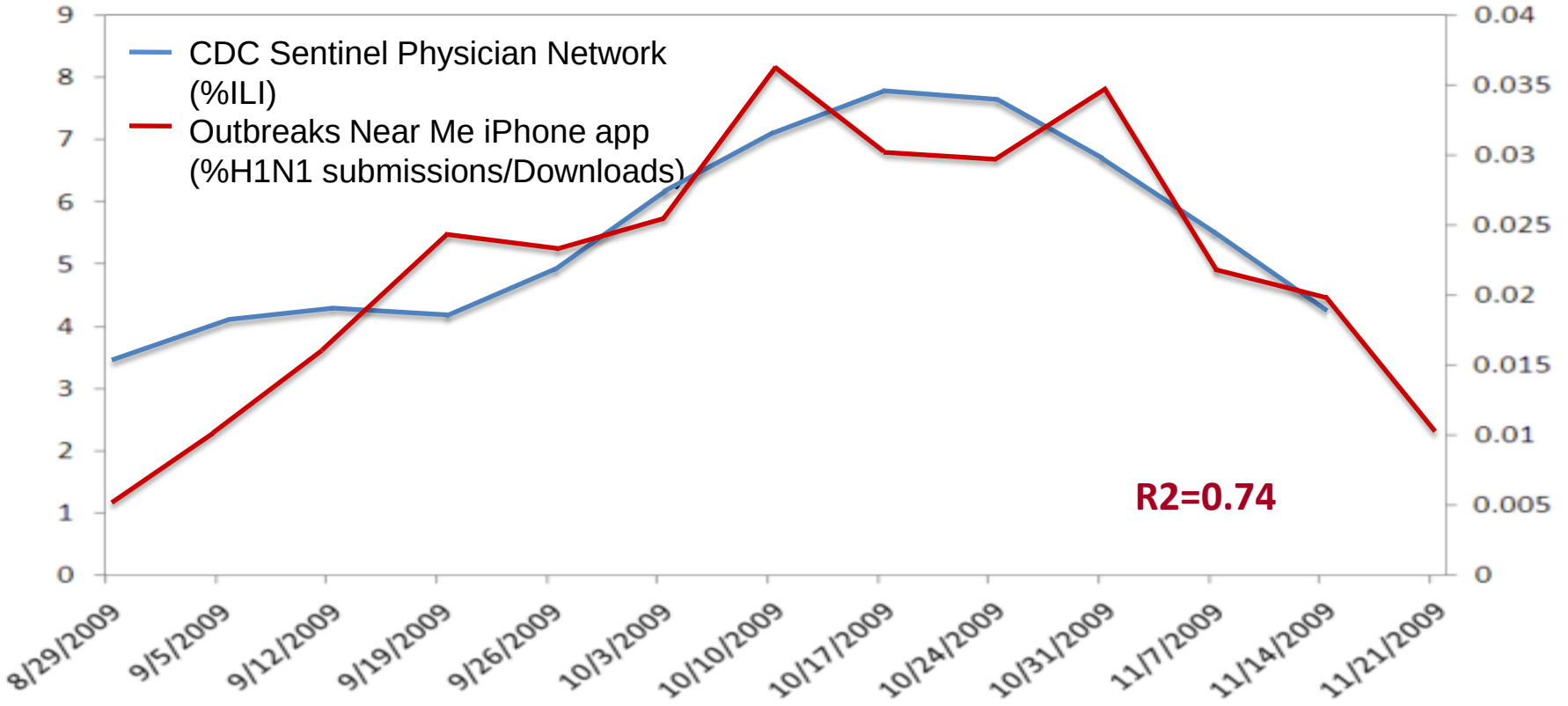
TIME
IN PARTNERSHIP WITH CNN

Wednesday, Sep. 09, 2009

Is a Swine Flu Outbreak Coming? Ask Your iPhone

By Bryan Walsh

iPhone Submissions vs CDC sentinel surveillance



CLARITY competition
(Crowdsourced discovery)

http://genes.childrenshospital.org

- Three families each with one affected child
- Nine exomes (Life) and genomes (CompleteGenomics)
- Three family clinical summaries
- $25K prize
- 30 international (commercial and academic) contest entrants!

Unexpected contest outcomes

Fast forward 10 years…

2023: Every patient encounter is learning opportunity (for provider and patient)

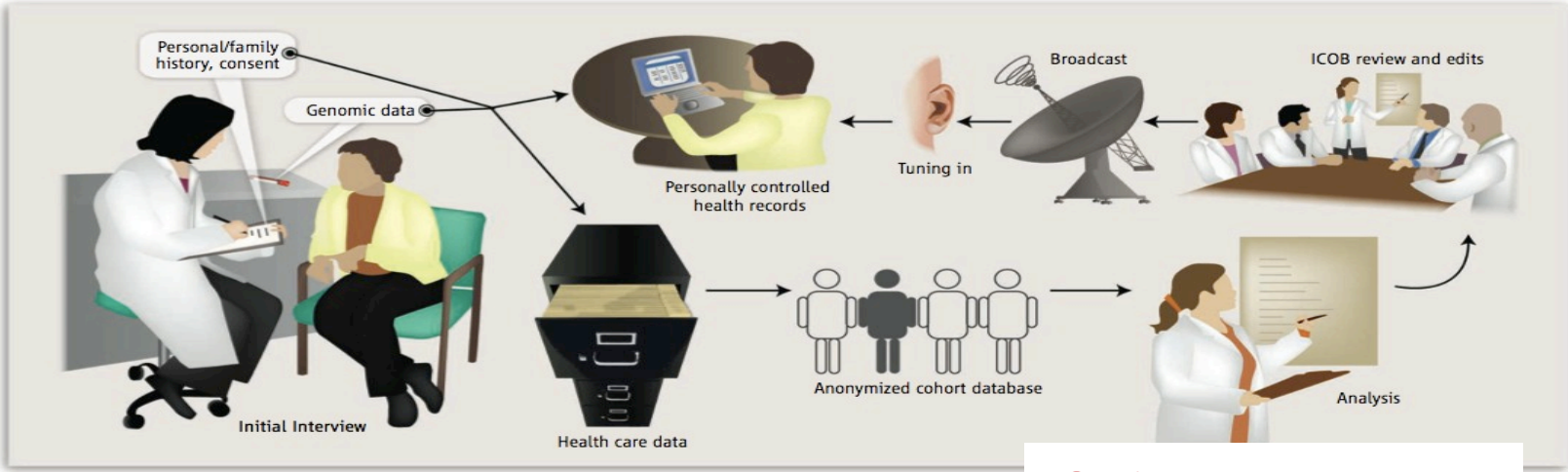
POLICYFORUM

MEDICINE

Reestablishing the Researcher-Patient Compact

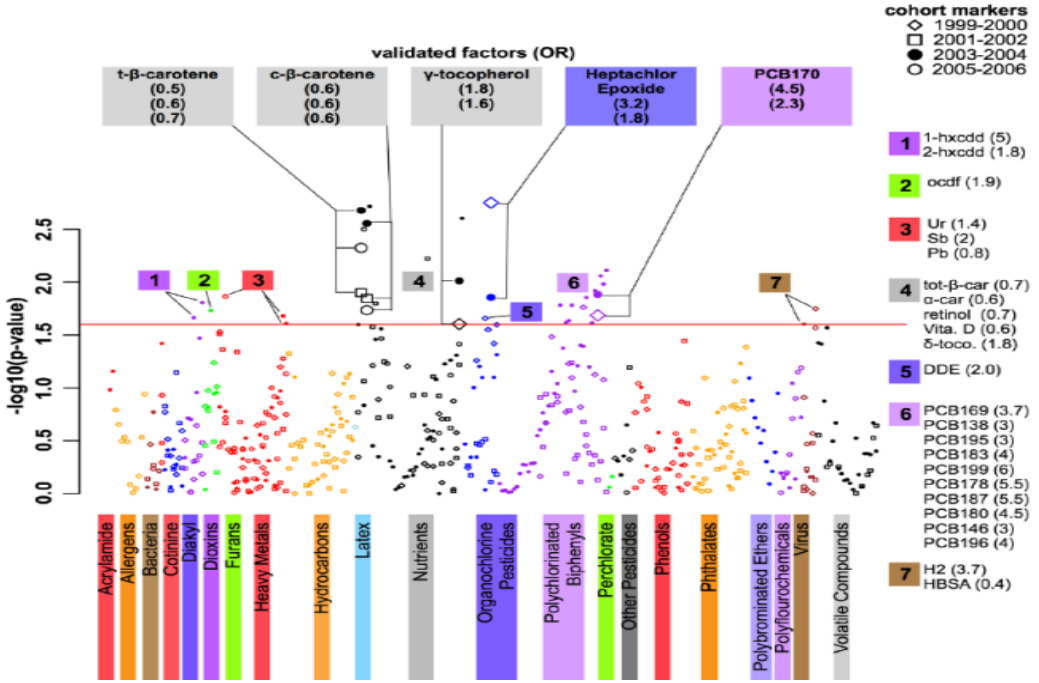
Isaac S. Kohane,[1,2,3]* Kenneth D. Mandl,[1,2,3] Patrick L. Taylor,[2,4] Ingrid A. Holm,[2,5] Daniel J. Nigrin,[1,2,3] Louis M. Kunkel[2,5,6]

Well-intentioned regulations protecting privacy are denying important information to patient subjects. Advances in information technology mean that a better approach to clinical research is possible.



Science 2007

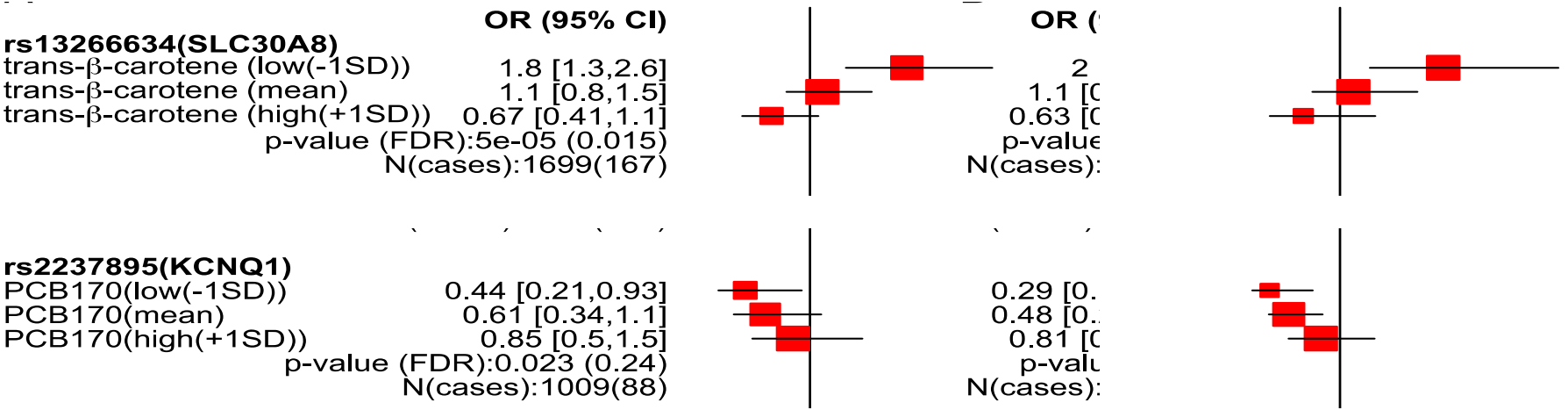
2023
Yearly check up includes exposure scan



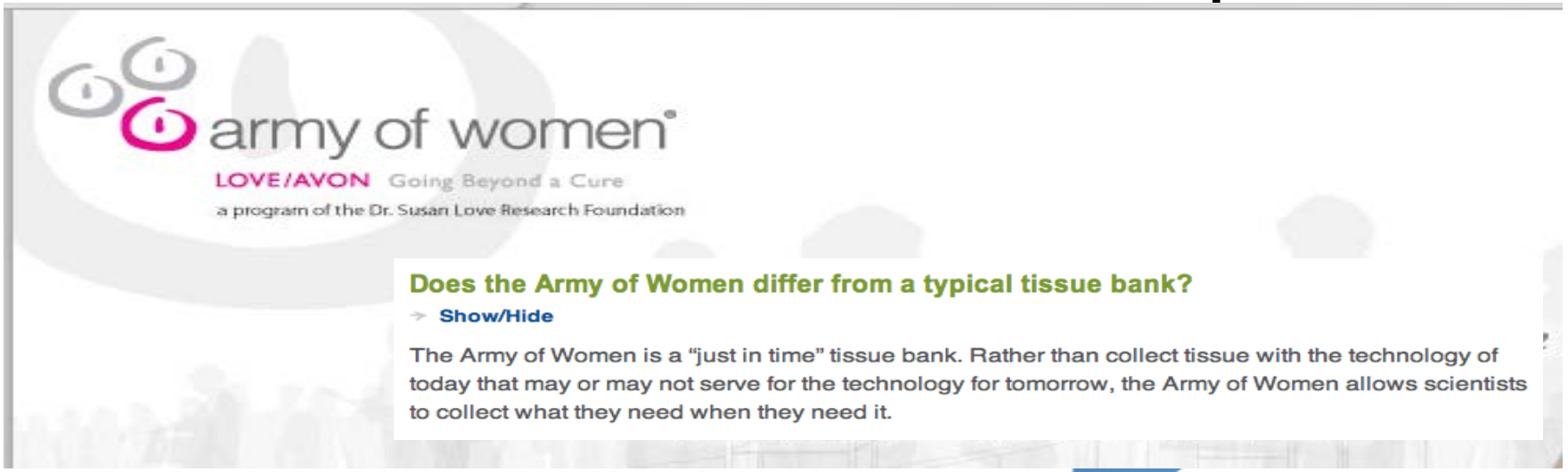
Patel C, Bhattacharya J, Butte AJ. *PLoS One*, 2010.

WGS data interpreted in light of interact with environmental factors and current clinical status.

Chirag Patel



Healthcare system no longer major source of trial patients.

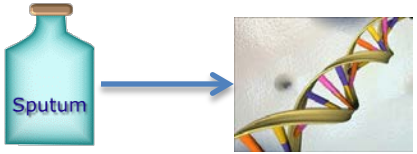


FlashTrials.gov/.com (*cf*. FlashMob) composed on the fly match volunteers to appropriate therapeutic trials. New study designs enable randomized partial trial participation.

In era of big data, well-characterized patients are the only non-commodity.

- WGS is no more expensive than electrolyte panel.
- BLUE button liquifies all data in any healthcare institution on behalf of the patient.
- Lifetime record is maintained by third party bonded data agency.
  - Includes everything we currently think of as health related but only the patient or guardian can provide access.

2023, more healthdata generated in 1 home than an ICU bed in 2013




Pathophys. Precis
• Nystagmus
• Diaphoresis
• Tropic Thunder
• Less than Zero
DDx
• ADHD
• Narcissism
• Terminal technophilia
Medications
• Blue pill
• Red pill
• Bitter pill
Social History
• Etoh+
• Nicotine+++
• WD40++++

What are the questions/challenges?

- Who is going to curate these data?
- What is the vector of FHx and genomic data?
- Is there a role for the healthcare system?
- How do we create a larger market for the information commons?
- What are we going to do to uniquely identify patients.

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smartplatforms.org

Developmental Medicine
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Chuck Nelson
Stephanie Brewster

Biotechnology
Daria Prilutsky
David Margulies

Genomics
Lou Kunkel
Alal Eran

Bioinformatics
Nathan Palmer
Patrick Schmid
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