

Precision Public Health at the Point of Care and for Patients at Home

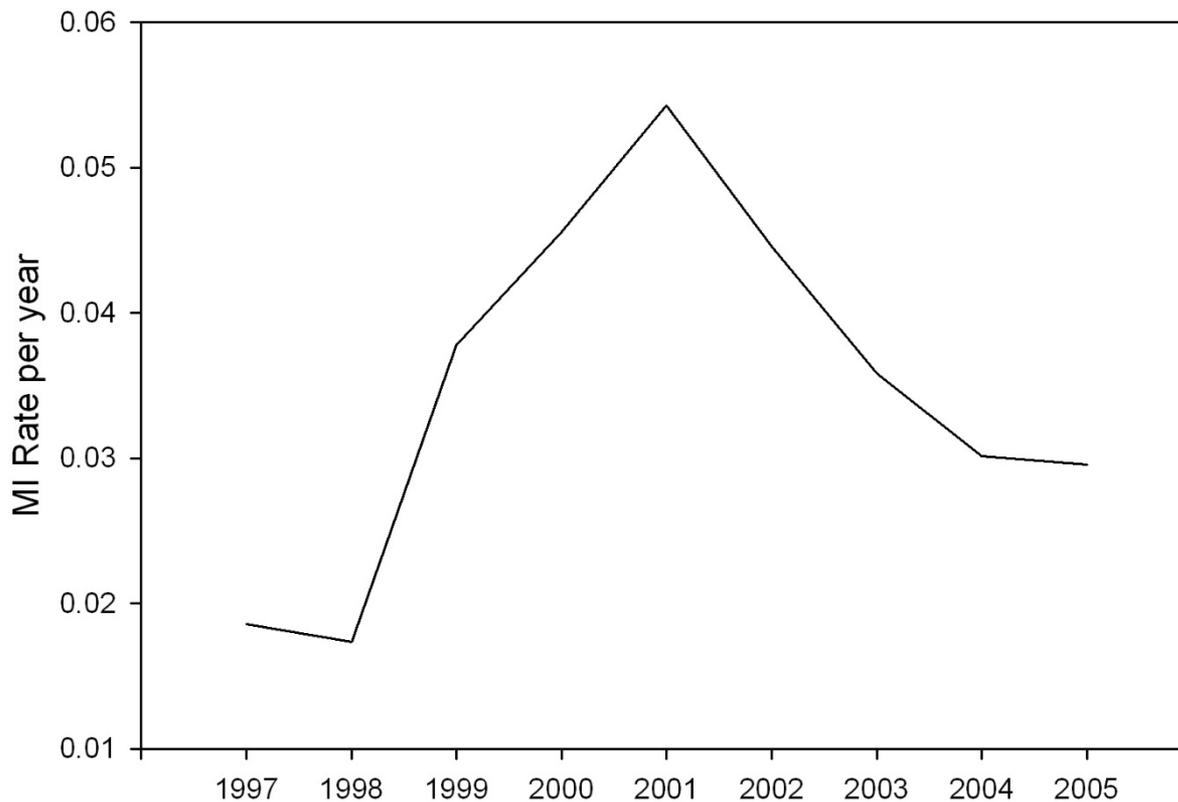
Kenneth D. Mandl, MD, MPH

Director, Computational Health Informatics Program
Boston Children's Hospital

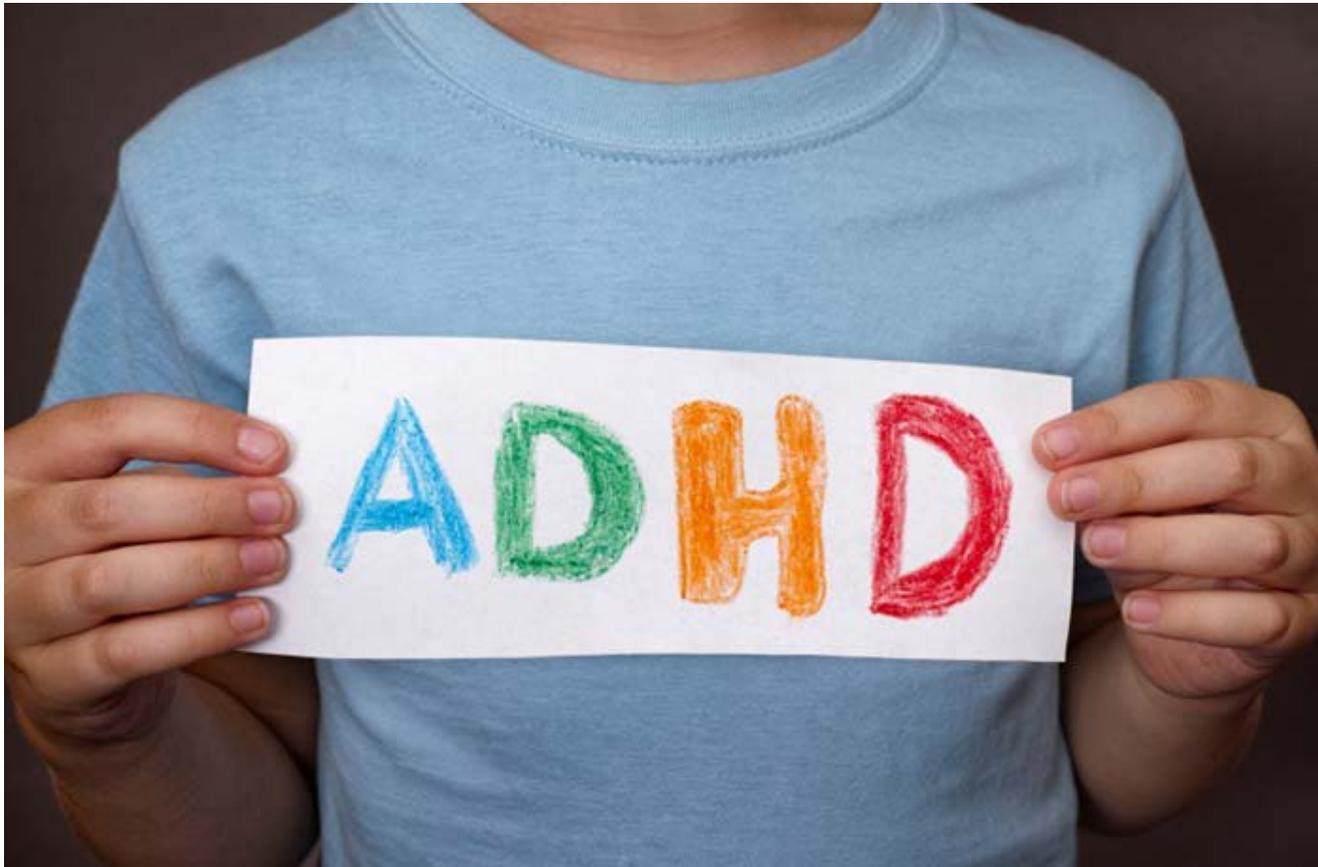
Donald A.B. Lindberg Professor of Pediatrics
Professor of Biomedical Informatics
Harvard Medical School

 @mandl

Case Study 1 - Imprecision at Scale



Case Study 2: Drug development



Case Study 3 - Genomic medicine



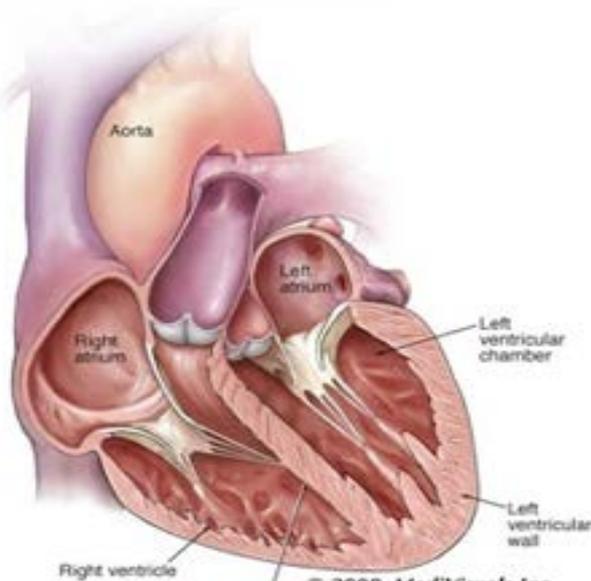
The NEW ENGLAND JOURNAL of MEDICINE

HOME	ARTICLES & MULTIMEDIA ▾	ISSUES ▾	SPECIALTIES & TOPICS ▾	FOR AUTHORS ▾	CME >
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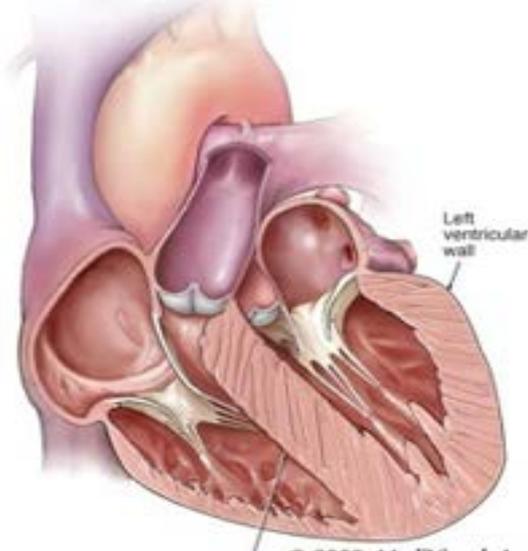
SPECIAL ARTICLE

Genetic Misdiagnoses and the Potential for Health Disparities

Normal Heart



Hypertrophic Cardiomyopathy



on, M.D., Peter Szolovits, Ph.D., David M.

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MEDIA IN THIS ARTICLE

FIGURE 1

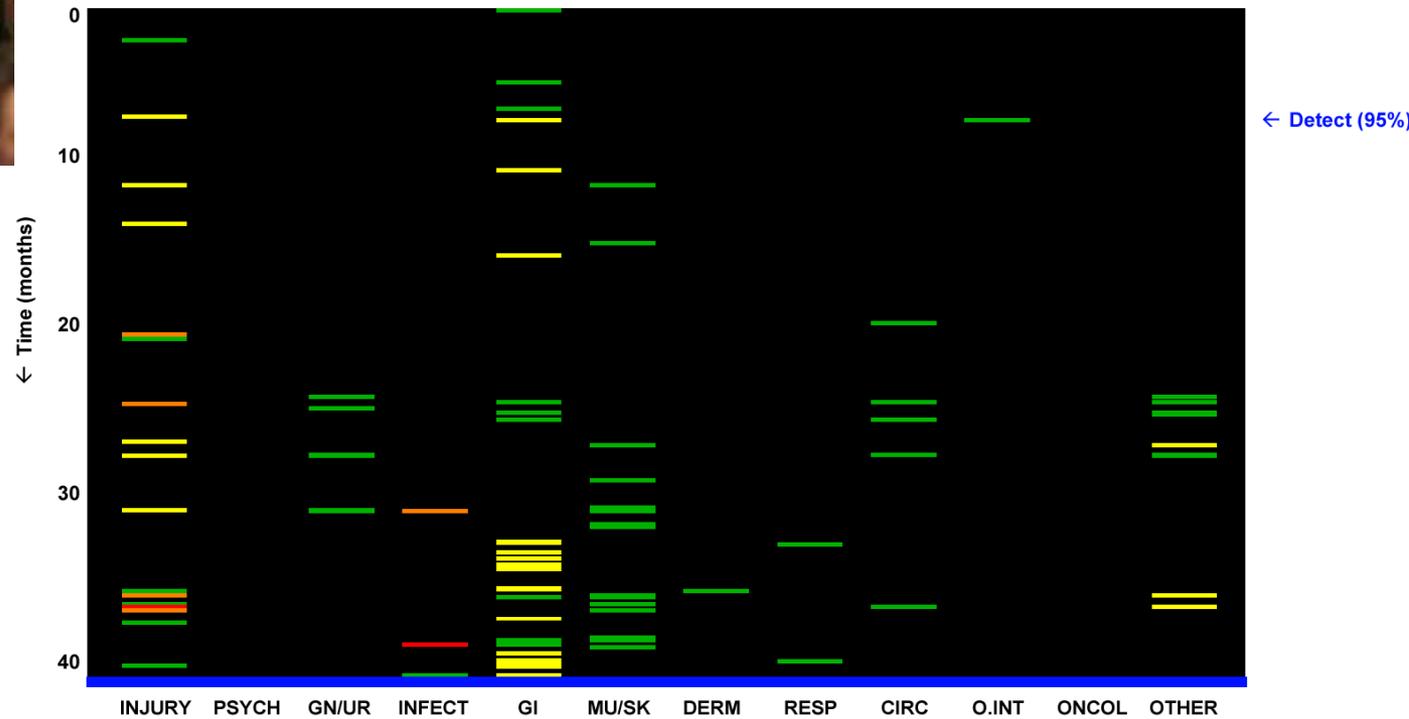
Case Study 4 - Image recognition

JAMA | **Original Investigation** | INNOVATIONS IN HEALTH CARE DELIVERY

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs



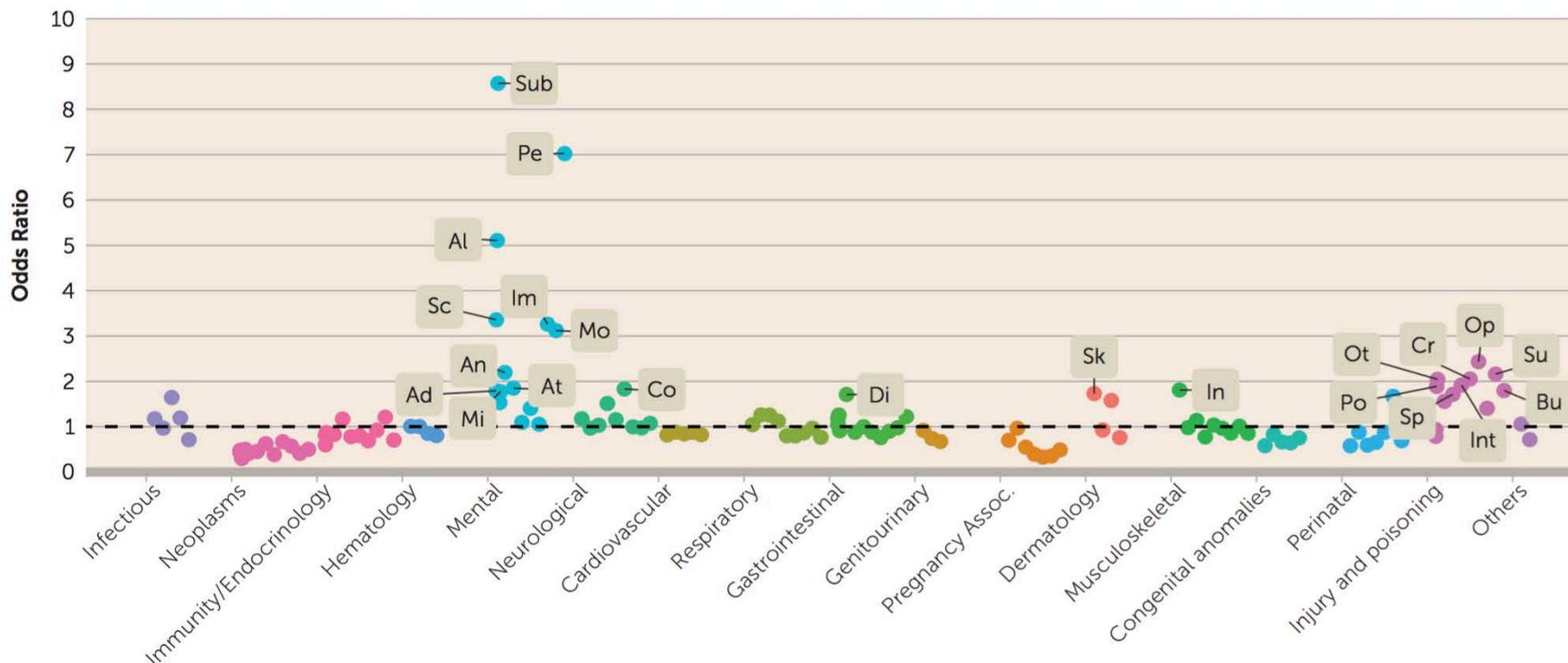
Case Study 5 - Predictive diagnostics



Domestic Violence

BMJ

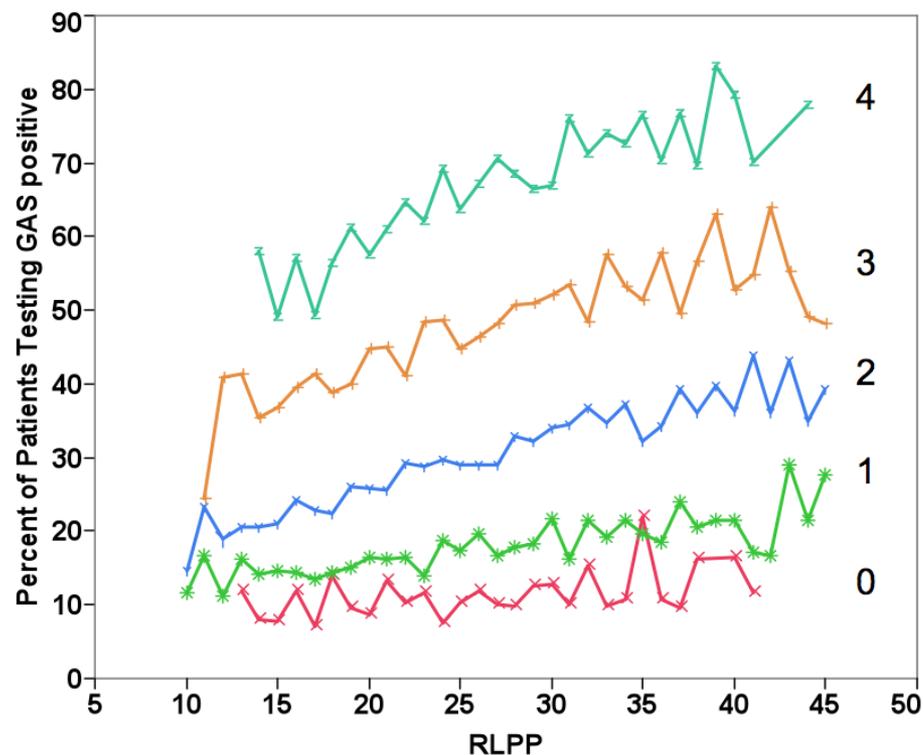
Case Study 5b - Predicting suicidal behavior



45% Sens, 95% spec, 3-4 years in advance

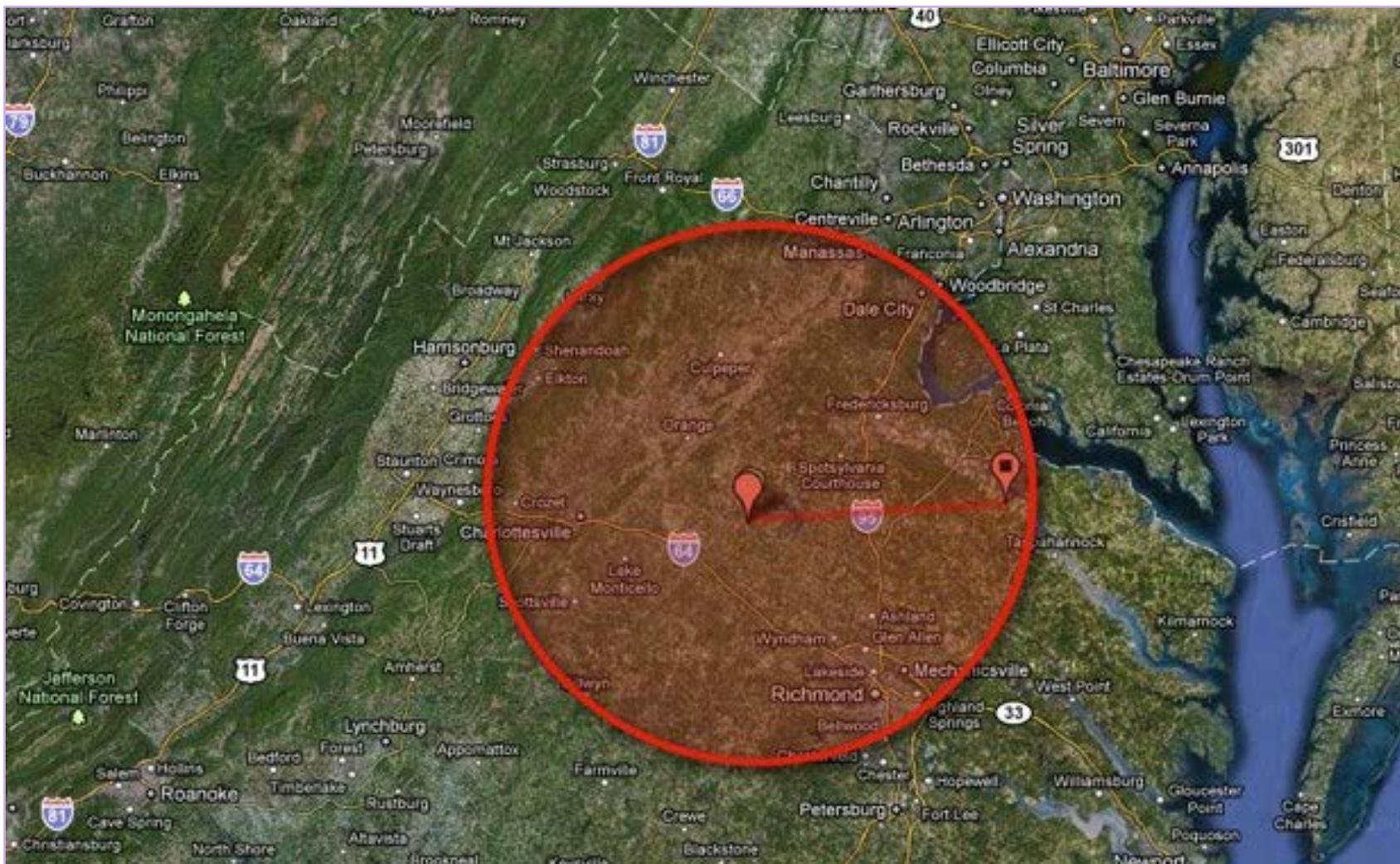


Case Study 6 - Adding context

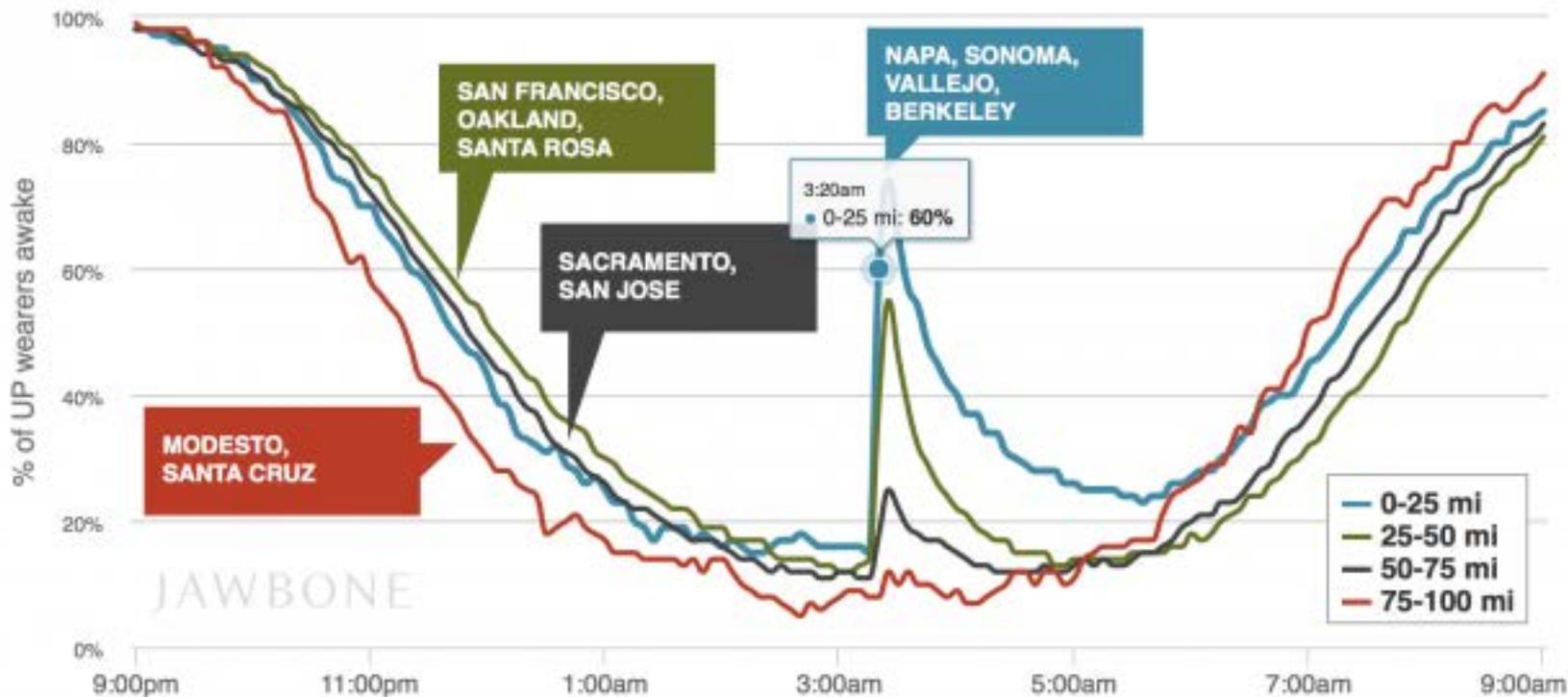


Annals of Internal Med

Virginia 2011

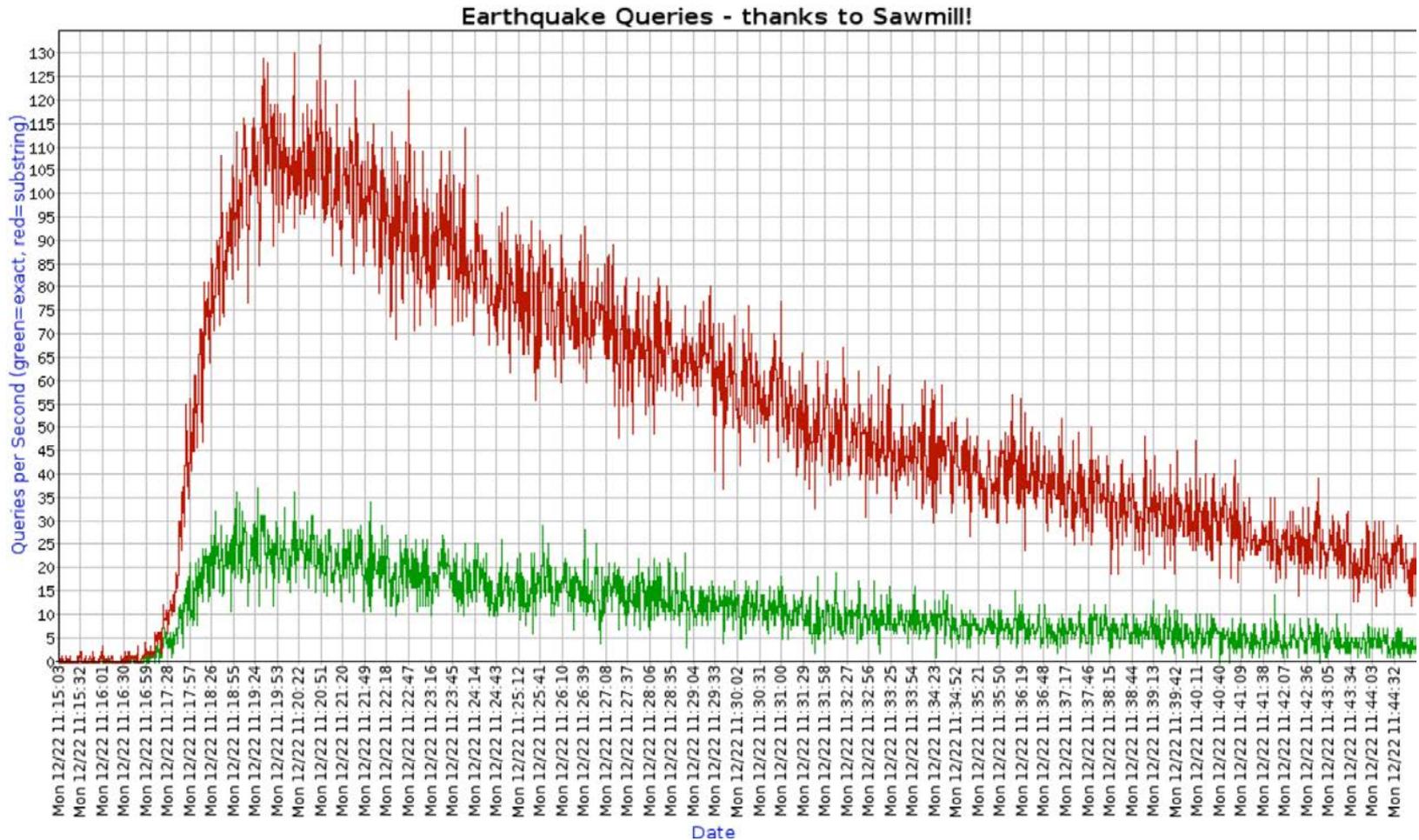


Earthquake detection, continued



We wish all the people in the Bay Area who were affected by the earthquake a speedy recovery and a good night's sleep.

Searching for quakes



AEGIS



HELP LOGOUT

CURRENTLY VIEWING: MASS - NEURO

SELECT DATE

Sun	Mon	Tue	Wed	Thu	Fri	Sat
—	—	17	18	19	20	21
22	23	24	25	26	27	28
29	30	1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19

SELECT HOSPITAL/SYNDROME Dec. 14, 2009

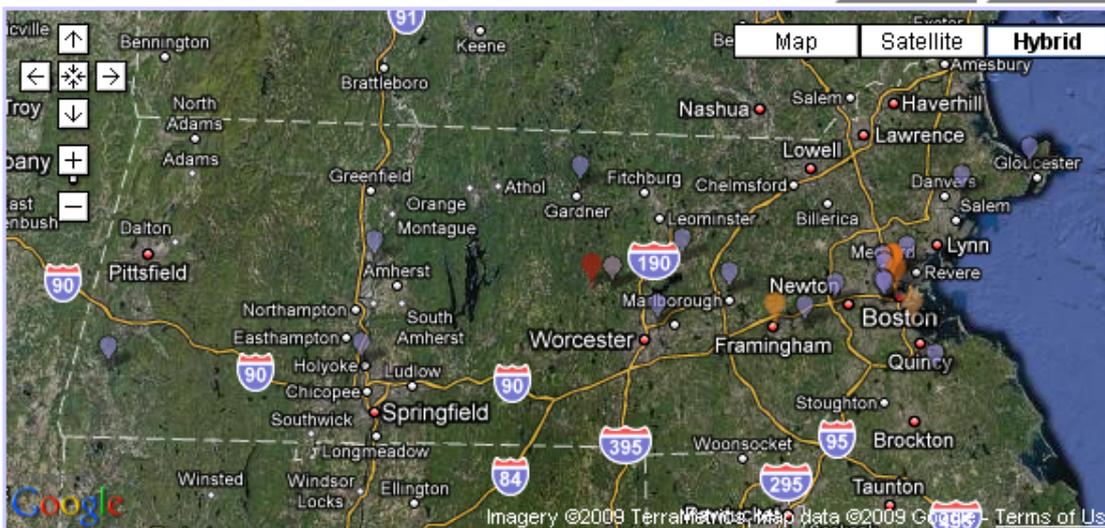
	NEURO	RESP	GI	RASH	HEMOR	ALL
MASS ?	■■■	■	■	■	■	■
E MA ?	■■■	■	■	■	■	■
C MA ?	■	■■■	■	■	■	■
W MA ?	■	■	■	■	■	■
AGH ?	■	■	■	■	■	■
BER ?	■	■	■	■	■	■
BEV ?	■■■	■	■	■	■	■

SELECT ABBERRATION
Aberrations For Current Selection

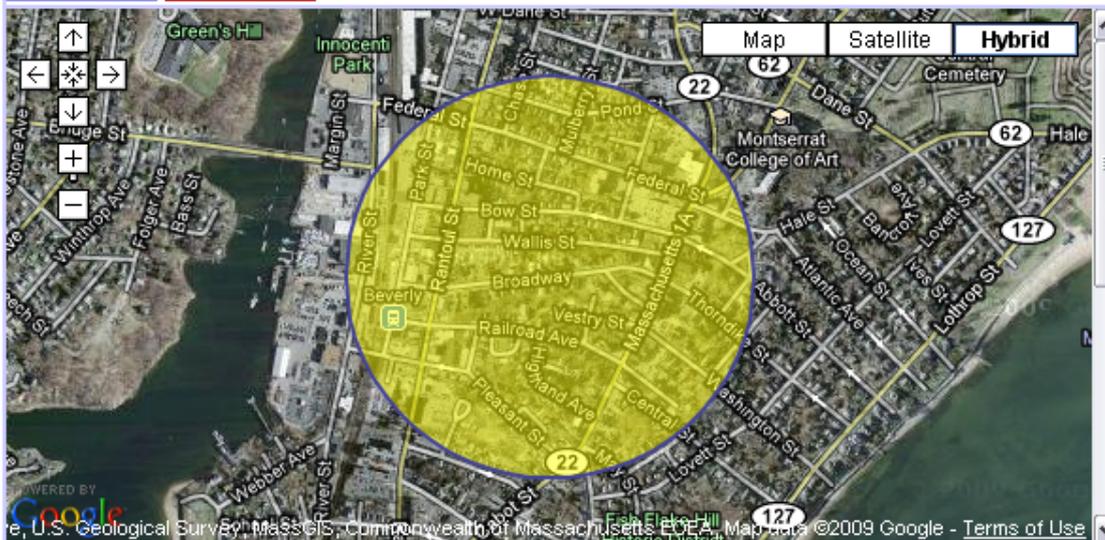
- MASS NEURO 12/14 [Explain](#)
- C MA RESP 12/14 [Explain](#)
- MGH RESP 12/2 [Explain](#)
- MASS NEURO 12/14 [Explain](#)
- MASS RESP 11/17 [Explain](#)
- MASS RESP 11/18 [Explain](#)
- MASS RESP 11/22 [Explain](#)

LEGEND

Active	Inactive	
■	■	- Normal
■■■	■■■	- Aberration (99% Certainty)
■■■	■■■	- Aberration (99.9% Certainty)
□	□	- Result not yet available



TEMPORAL SPATIAL



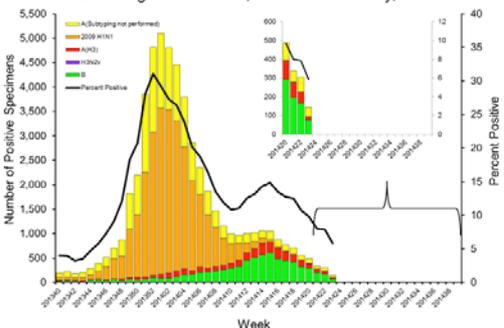
Combining information from **multiple data** sources real-time monitoring becomes more accurate and robust.

Our methods perform better than now-discontinued Google Flu Trends tool

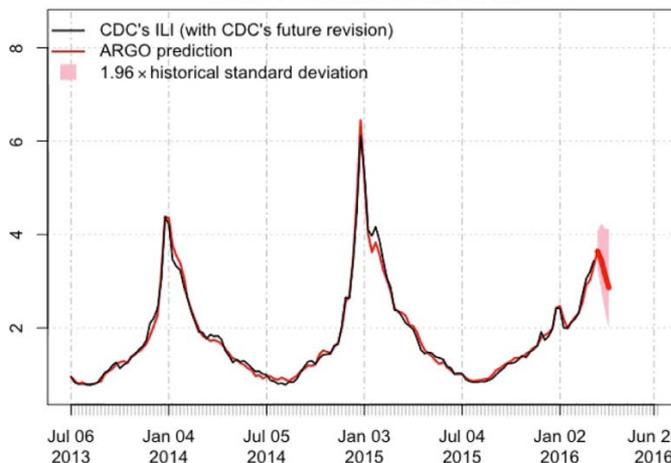


CENTERS FOR DISEASE CONTROL AND PREVENTION

Influenza Positive Tests Reported to CDC by U.S. WHO/NREVSS Collaborating Laboratories, National Summary, 2013-14



ARGO Prediction vs. CDC's ILI



2017/2018

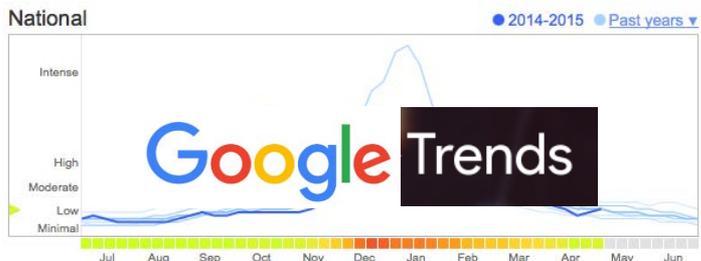
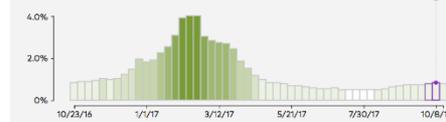
FLU SEASON

Week 41

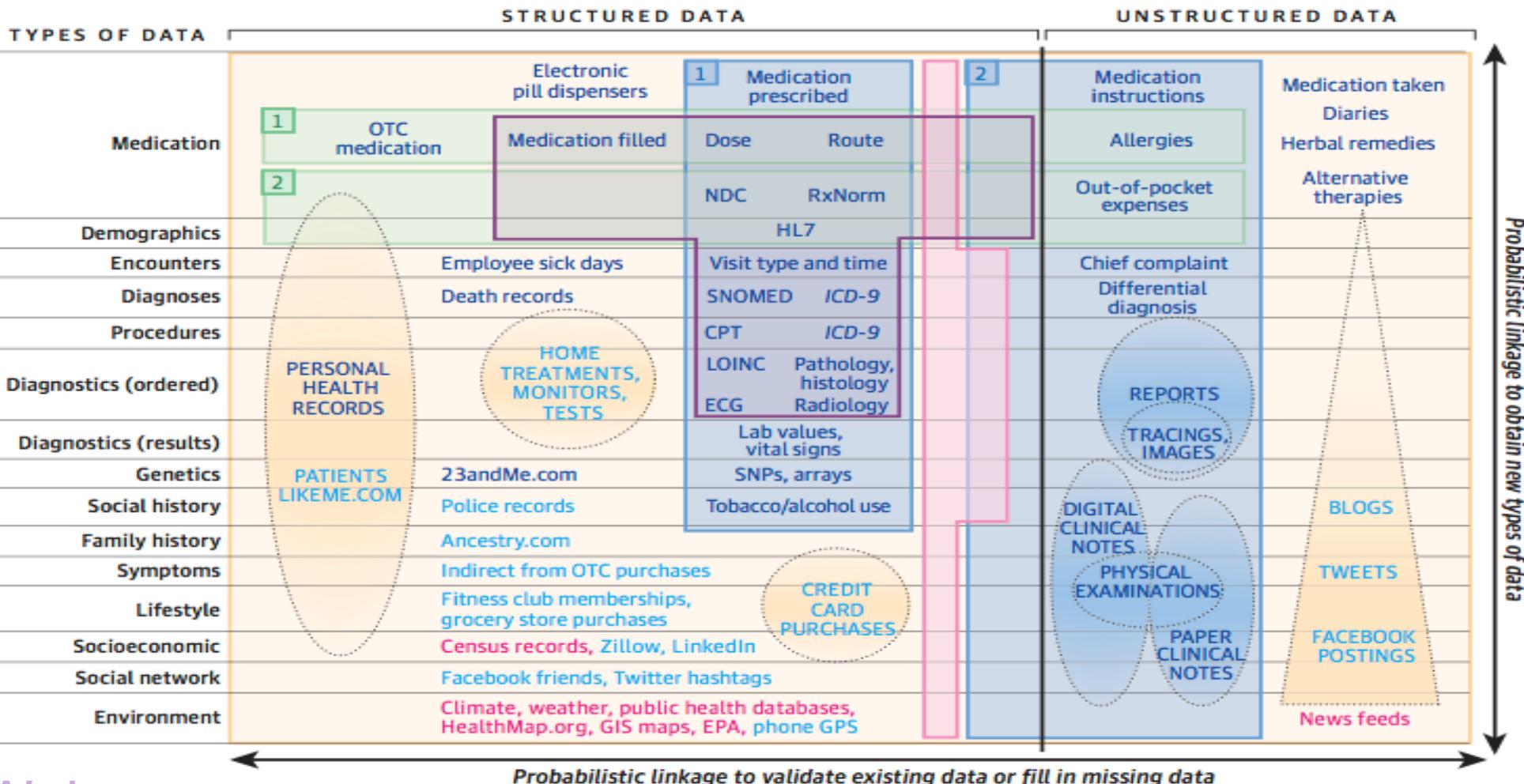
Oct 8 - Oct 14, 2017

US Average

0.82%



The Tapestry of Potentially High-Value Information Sources That May be Linked to an Individual for Use in Health Care



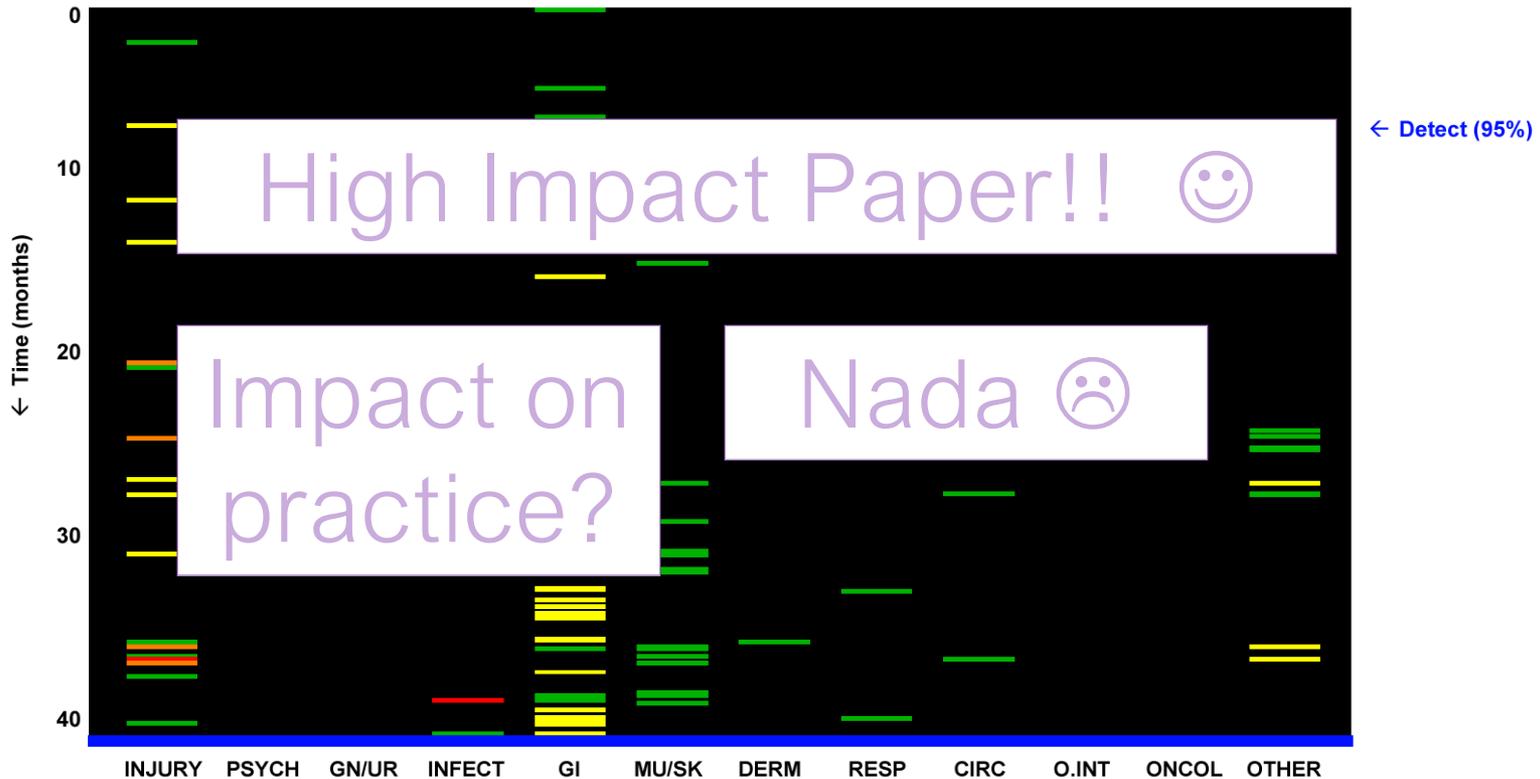
Probabilistic linkage to validate existing data or fill in missing data

Probabilistic linkage to obtain new types of data

Weber,
Mandl,
Kohane

Examples of biomedical data		Ability to link data to an individual		Data quantity
<div style="border: 1px solid green; padding: 2px;">1</div> Pharmacy data	<div style="border: 1px solid blue; padding: 2px;">1</div> Health care center (electronic health record) data	■ Easier to link to individuals	■ Harder to link to individuals	<div style="border: 1px dashed orange; width: 20px; height: 10px;"></div> More
<div style="border: 1px solid purple; padding: 2px;"></div> Claims data	<div style="border: 1px solid pink; padding: 2px;"></div> Registry or clinical trial data	■ Only aggregate data exists		<div style="border: 1px solid blue; width: 20px; height: 10px;"></div> Less
<div style="border: 1px solid orange; padding: 2px;"></div> Data outside of health care system				

Predictive Medicine: Domestic Violence



BMJ

Turns out it matters

JAMA The Journal of the
American Medical Association

Viewpoint | October 20, 2014 **FREE**



Ebola in the United States: EHRs as a Public Health Tool at the Point of Care

Kenneth D. Mandl, MD, MPH

This Viewpoint discusses how health information technology and electronic health records (EHRs) could be transformed into platforms for public health responses to disease.

Topics: ebola virus; ebola virus disease; public health medicine; electronic medical records

JAMA. Published online October 20, 2014. doi:10.1001/jama.2014.15064



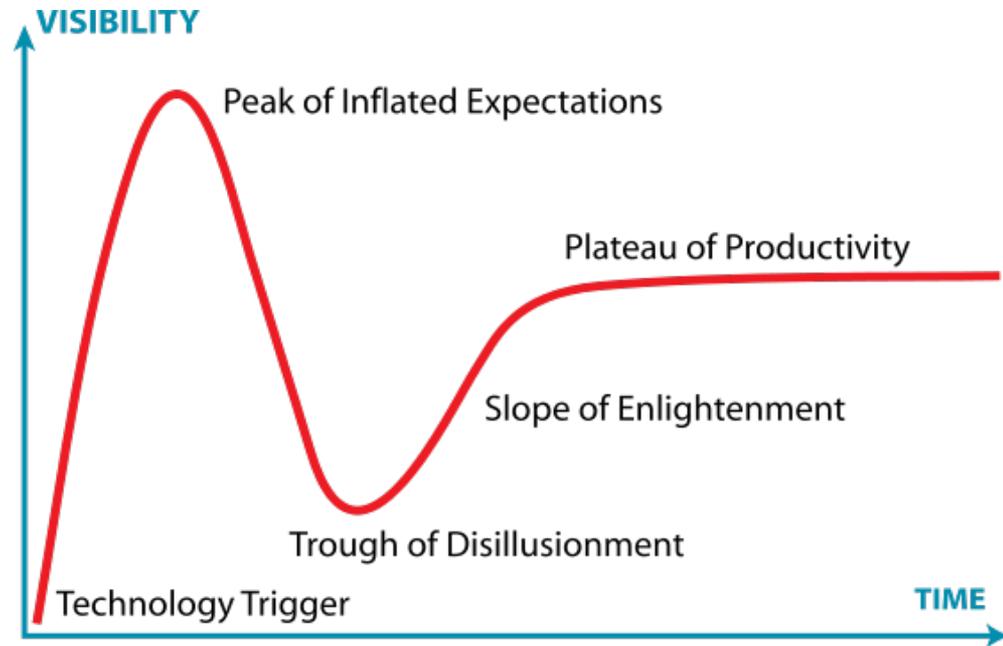
- Precision requires computation.
- Computation requires data. A lot of data.
- Researchers struggle to amass the data they need.
- Clinicians have very little data at their fingertips when treating patients.
- Public health data assets are not well-integrated into the point of care
- A new class of patient/parent leaders and scientists are at the forefront of understanding these needs and are breaking down the barriers.

DATA ARE NOT INTEROPERABLE



Hype Curve and HIT

- \$48B US investment in HIT
- >\$2B at Partners
- >\$0.5T total



Point of care is a walled garden





The NEW ENGLAND JOURNAL of MEDICINE

No Small Change for the Health Information Economy

Kenneth D. Mandl, M.D., M.P.H., and Isaac S. Kohane, M.D., Ph.D.

The economic stimulus package signed by President Barack Obama on February 17 included a \$19 billion investment in health information technology. How can we best take advantage of this unprecedented opportunity to computerize health care and stimulate the health information economy while also stimulating the U.S. economy? A health care system adapting to the effects of an aging population, growing expenditures, and a diminishing primary care workforce needs the support

of a flexible information infrastructure that facilitates innovation in wellness, health care, and public health.

Flexibility is critical, since the system will have to function under new policies and in the service of new health care delivery mechanisms, and it will need to incorporate emerging information technologies on an ongoing basis. As we seek to design a system that will constantly evolve and encourage innovation, we can glean lessons from large-scale information-

technology successes in other fields. An essential first lesson is that ideally, system components should be not only interoperable but also substitutable.

The Apple iPhone, for example, uses a software platform with a published interface that allows software developers outside Apple to create applications; there are now nearly 10,000 applications that consumers can download and use with the common phone interface. The platform separates the system from the functional-

'API'



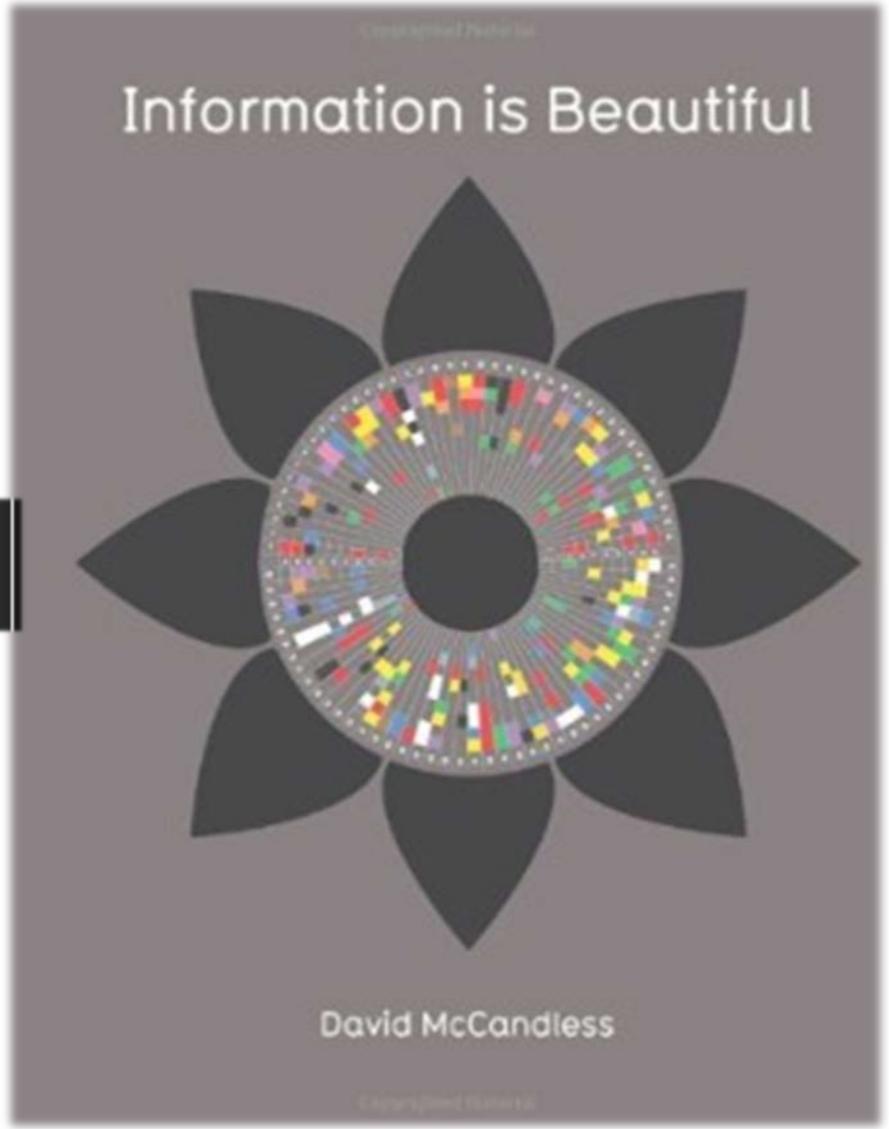
Can EMRs behave like iPhones or Androids in that innovators readily create and widely distribute **SUBSTITUTABLE** apps across thousands of installs?

Inspired by a

WIRED

18.12 Issue

Design Challenge



State-of-the-art ???

<input checked="" type="checkbox"/> ALIGN HERE		SEND TO:					
PATIENT NAME DOE, JOE			PATIENT ID NO. NOT GIVEN		DATE COLLECTED	TIME	
ACCESSION NO. 36904447	BIRTH DATE 55	GENDER MALE	SAMPLE ID NO. NOT GIVEN	OTHER ID NO.	RECEIVED 06/11/2010	09:41	
REMARKS SAMPLE REPORT, NO SAMPLE SENT				REFERRING PHYSICIAN	REPORTED 06/11/2010	10:00	
					STATUS FINAL		
TEST	RESULT (* = OUT OF RANGE)		UNITS		REFERENCE RANGE		
Cardio CRP			0.4 mg/L				
For Ages > 17 Years:							
CCRP mg/L	Risk According to AHA/CDC Guidelines						
<1.0	Lower Relative Cardiovascular Risk.						
1.0-3.0	Average Relative Cardiovascular Risk						
3.1-10.0	Higher Relative Cardiovascular Risk. Consider retesting in 1 to 2 weeks to exclude a benign transient elevation in the baseline CRP value secondary to infection or inflammation.						
>10.0	Persistent elevations upon retesting, may be associated with infection and inflammation.						

Bloodwork Cardiology Result


 BACTA MEDICAL CENTRE

ORDERED BY: Dr. Francis Pulaski
 Bellevue Medical Centre
 lamar.d@bactamed.edu
 (603) 555-54321 x1523
 COLLECTED: 11/02/2010, 10:40 a.m.
 RECEIVED: 11/02/2010, 1:03 p.m.

Patient info

NAME: **John Doe**
 GENDER: M AGE: 49 DOB: 01/10/1961

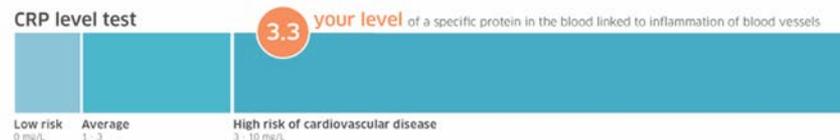
An Inspired Design from Dave McCandless (cc license)

1 About this test

This report evaluates your potential risk of heart disease, heart attack, and stroke.

2 Your results

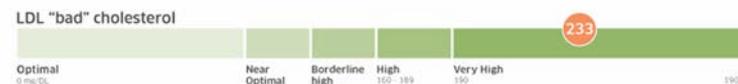
CRP level test



Total cholesterol level



LDL "bad" cholesterol



HDL "good" cholesterol



3 Your risk You show an elevated risk of cardiovascular disease

If you're a smoker with normal blood pressure, (130 mm/Hg) but family history of heart attack before age 60 (one or both parents) your risk over 10 years is:

15%

Your risk would be lowered to

12% if your blood pressure were 120mm/Hg
10% if you quit smoking
6% if you reduced cholesterol to 160mg/DL

Use your CRP results and cholesterol level to calculate your 10 risk of a cardiovascular event at ReynoldsRisk.org

4 What now?



Diet & exercise- can improve your cholesterol levels



Quitting smoking- can decrease your heart disease risk by 50% or more

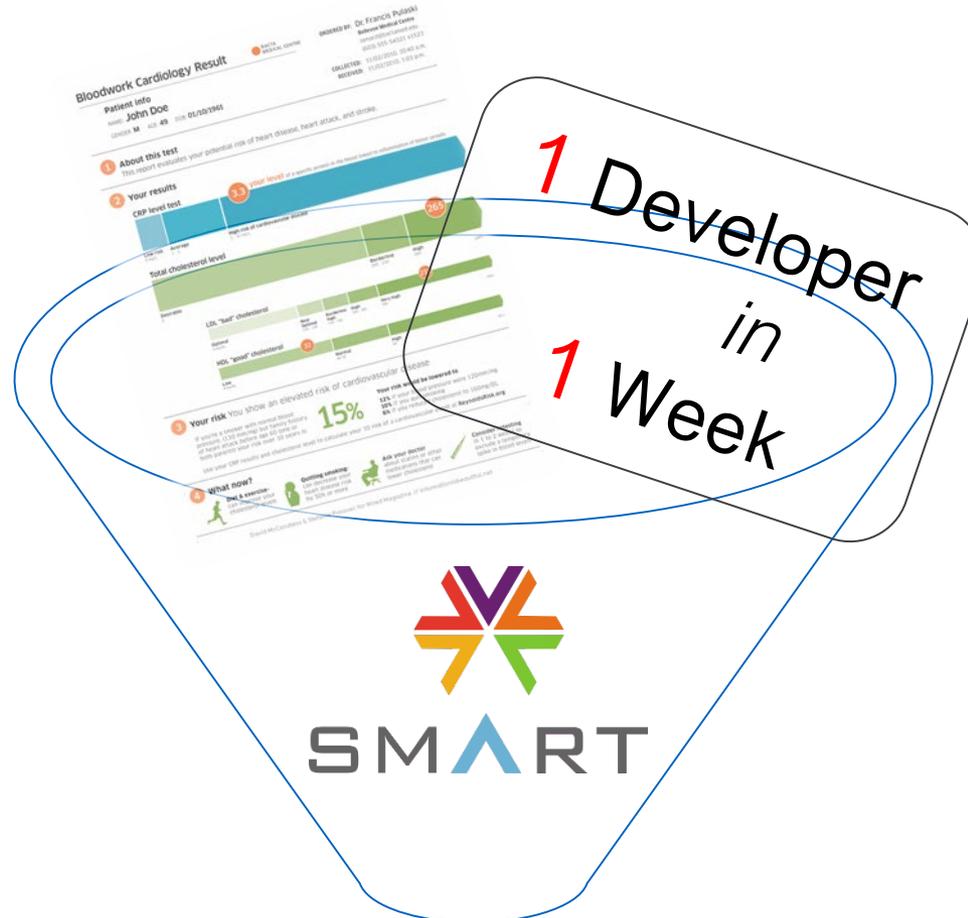


Ask your doctor about statins or other medications that can lower cholesterol



Consider retesting in 1 to 2 weeks to exclude a temporary spike in blood levels

1 Design + 1 Developer + 1 Week



SMART
Cardiac
Risk
App

1 SMART app in 3 SMART systems



Indivohealth™ for John Smith

SETTINGS LOGOUT

Mary | John S. Smith | Joshua Lewis

Bloodwork Cardiology Result

Patient info: **Joshua Lewis**
 GENDER: M AGE: 71 DOB: 1939-09-12
 Current smoker?
 Family history of heart attack?
 Systolic blood pressure

1 About this test
 This report evaluates your potential risk of heart disease, heart attack, and stroke.

2 Your Results

CRP level test
 2.4
 Low risk: 0-1.0 | Average: 1.1-3.0 | High risk of cardiovascular disease: 3.1-10.0

Total cholesterol level
 141
 Desirable: 0-199 | Borderline: 200-239 | High: 240+

LDL "bad" cholesterol
 81
 Desirable: 0-100 | Borderline: 101-159 | High: 160-199 | Very High: 200+


 SMART

Patient List
 Cardiac Risk
 Clinical Research
 Dietsocial
 Most Risk Maps
 Medication
 MyNotes

Alex Lewis
 NAME: Alex Lewis
 GENDER: M AGE: 71 DOB: 1939-09-12

Note: these results are valid for non-diabetic only!
 Current smoker?
 Family history of heart attack?
 Systolic blood pressure

1 About this test
 This report evaluates your potential risk of heart disease, heart attack, and stroke.

2 Your Results

CRP level test
 2.4
 Low risk: 0-1.0 | Average: 1.1-3.0 | High risk of cardiovascular disease: 3.1-10.0

Total cholesterol level
 141
 Desirable: 0-199 | Borderline: 200-239 | High: 240+

LDL "bad" cholesterol
 107
 Desirable: 0-100 | Borderline: 101-159 | High: 160-199 | Very High: 200+

HDL "good" cholesterol
 34
 Low: 0-49 | Normal: 50-129 | High: 130-159

3 Your risk You show an elevated risk of cardiovascular disease
 If you're a smoker with normal blood pressure (130 mm/Hg) but family history of heart attack before the age of 60 (one or both parents) your risk over 15 years is:
12% Your risk would be lowered to:
3% if you didn't smoke and all levels were optimal
32% if you quit smoking.
 Use your test results to calculate your risk of a cardiovascular event at ReynoldsRisk.org

4 What now?

CHIP - HMS - © 2011

Indivohealth™ for John Smith
 Mary | John S. Smith | Joshua Lewis

Bloodwork Cardiology Result

Patient info: **Joshua Lewis**
 GENDER: M AGE: 71 DOB: 1939-09-12
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 Use your test results to calculate your risk of a cardiovascular event at ReynoldsRisk.org

4 What now?

SMART

- Patient List
- Cardiac Risk
- Clinical Research
- DxSocial
- Med Risk Maps
- Meducation
- MyNote

< Alex Lewis > Challenge Judge

Med List CMI Demos English Regular

Meducation
www.meducation.com
0 1 W K G V 3 R

Pharmacy
Health & Wellness
Polyglot Systems, Inc.
2000 Aerial Center Parkway
Morrisville, NC 27560
(919) 653-4392

Coumadin Tablet 5 mg

How to take medicine
Take the medicine by mouth once a day.

Breakfast	Lunch	Dinner	Bedtime
1			

Take one (1) pill each time.

Instructions
Swallow the medicine without crushing or chewing it.
This medicine may be taken with or without food.
It is very important that you take the medicine at about the same time every day. It will work best if you do this.

< Alex Lewis > Challenge Judge

Med List CMI Demos Spanish Regular

Meducation
www.meducation.com
0 2 W K G V 3 R

Pharmacy
Health & Wellness
Polyglot Systems, Inc.
2000 Aerial Center Parkway
Morrisville, NC 27560
(919) 653-4392

Coumadin Tablet 5 mg

Cómo tomar el medicamento
Tome el medicamento por la boca una vez al día.
Take the medicine by mouth once a day.

Desayuno	Almuerzo	Comida	Al acostarse
1			

Tome una (1) pastilla cada vez.
Take one (1) pill each time.

Instrucciones
Trague el medicamento sin aplastarlo o masticarlo.
Este medicamento se puede tomar con o sin alimentos.

Indivohealth™ for John Smith

SETTINGS LOGOUT

Mary | John S. Smith | Joshua Lewis

- Healthfeed
- Inbox
- Cardiac Risk
- DxSocial
- MyNote
- Meducation
- Sharing
- Get more apps
- App Settings

Med List CMI Demos Spanish Regular

Meducation
www.meducation.com
0 2 E 6 H G U 6

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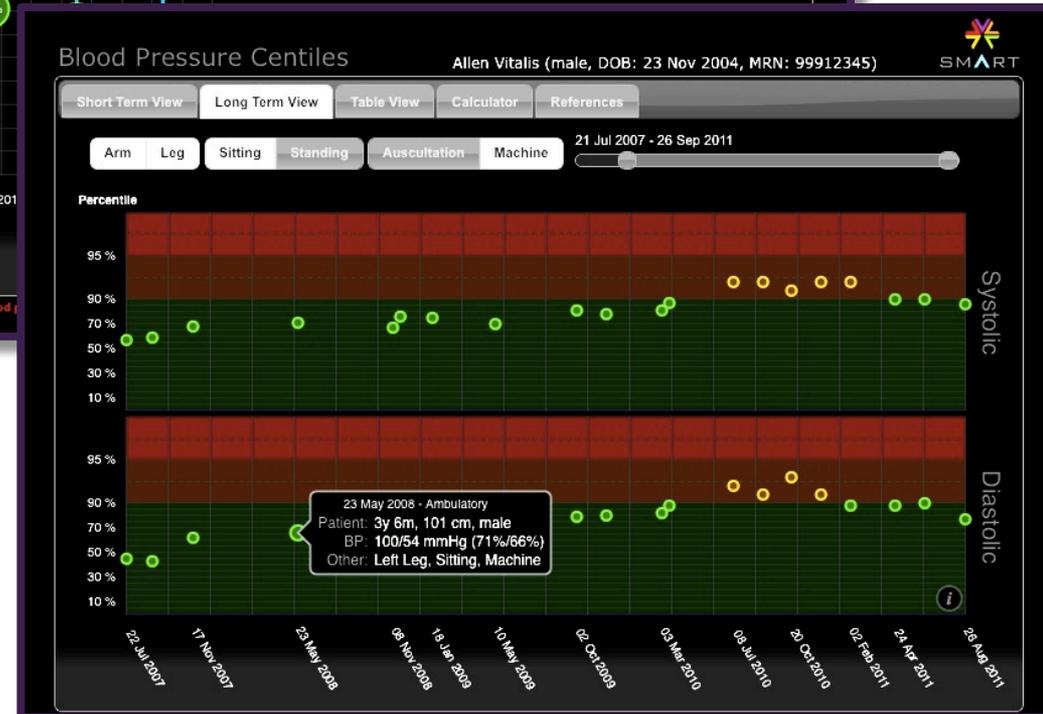
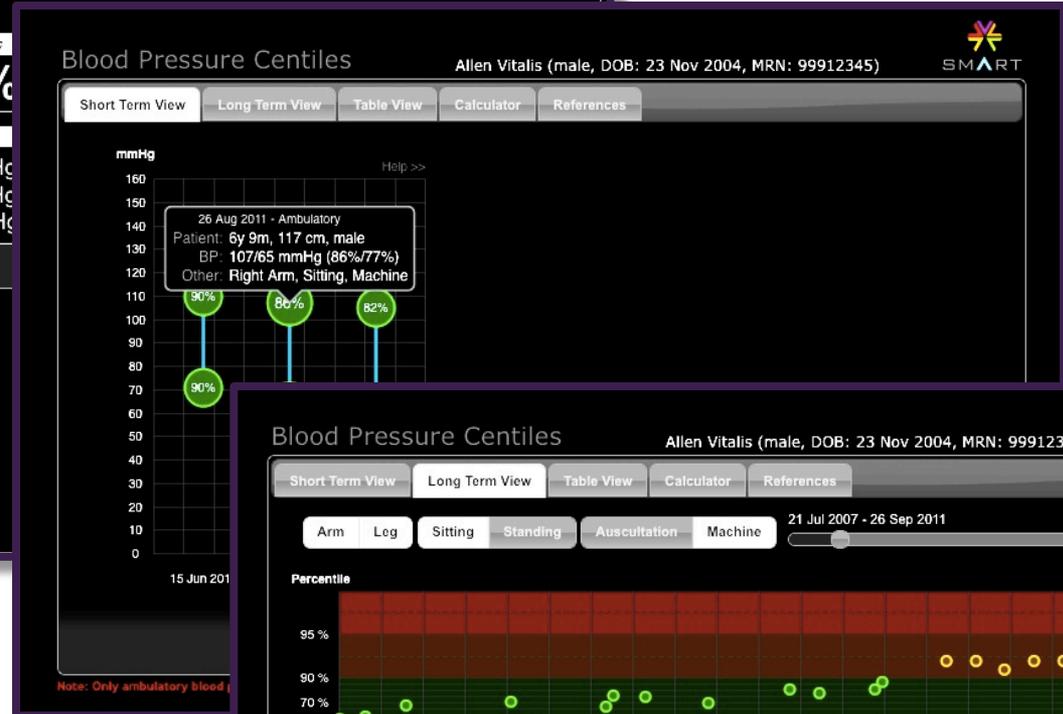
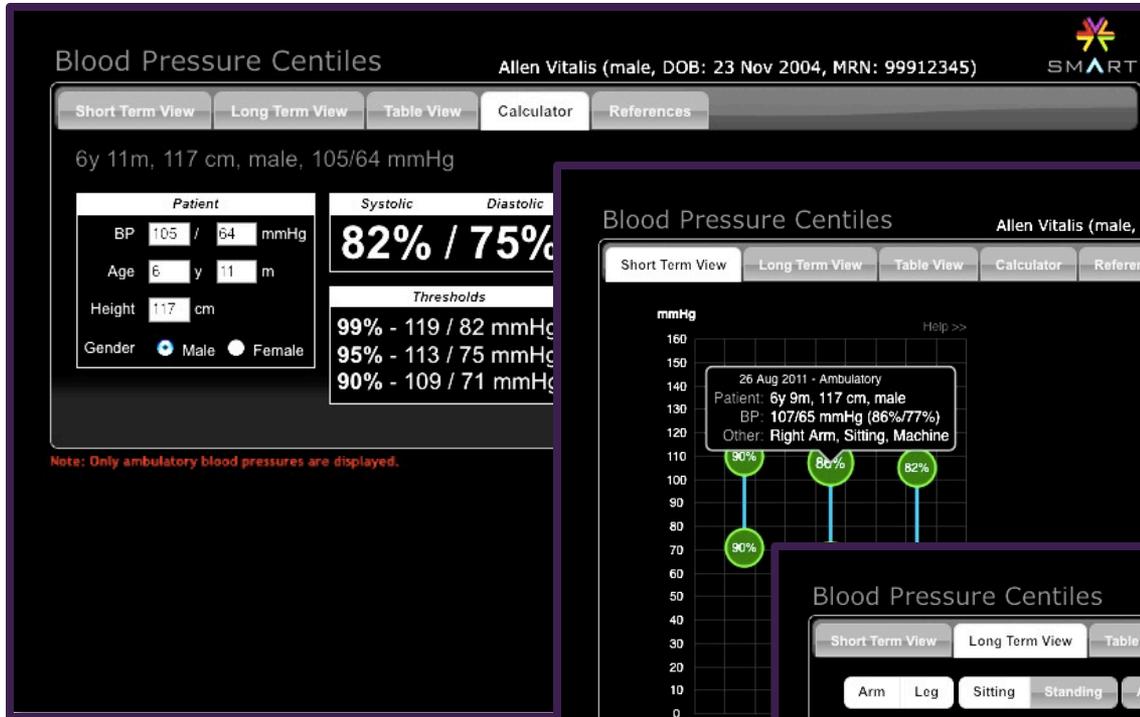
Coumadin Tablet 5 mg

Cómo tomar el medicamento
Tome el medicamento por la boca una vez al día.
Take the medicine by mouth once a day.

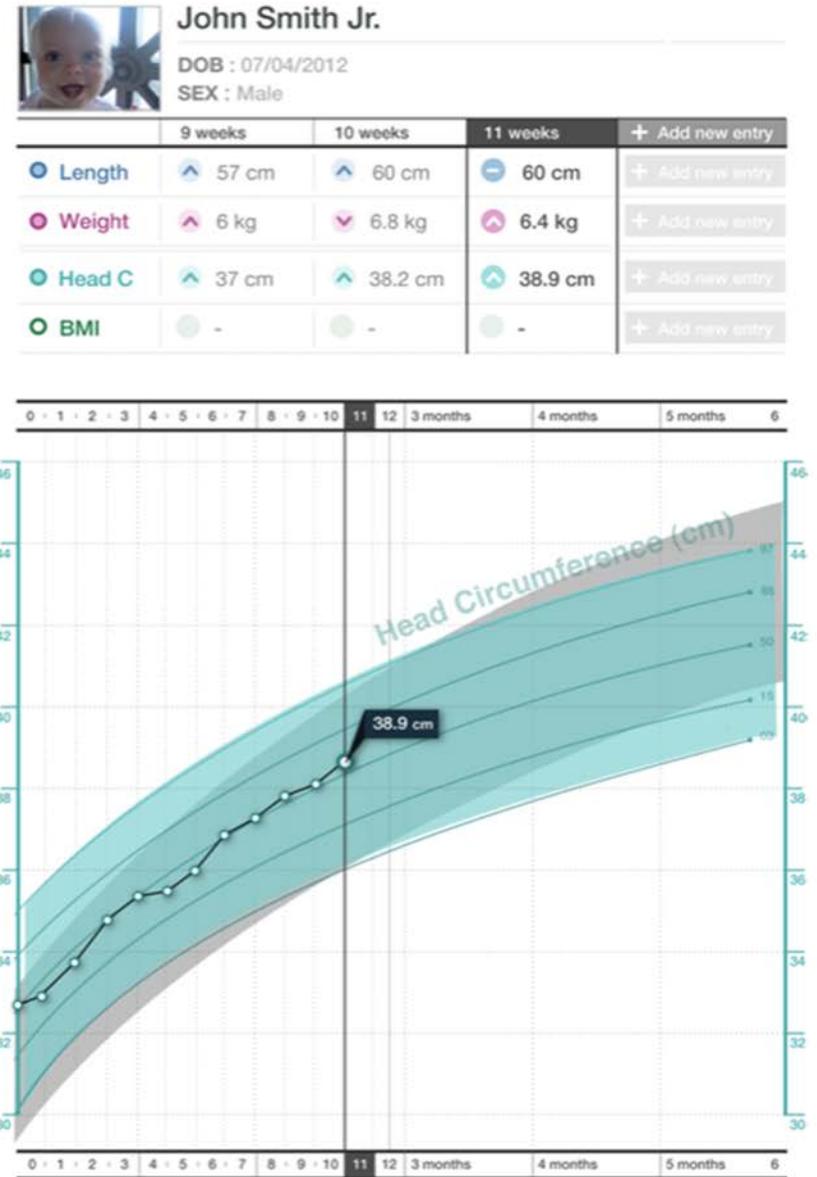
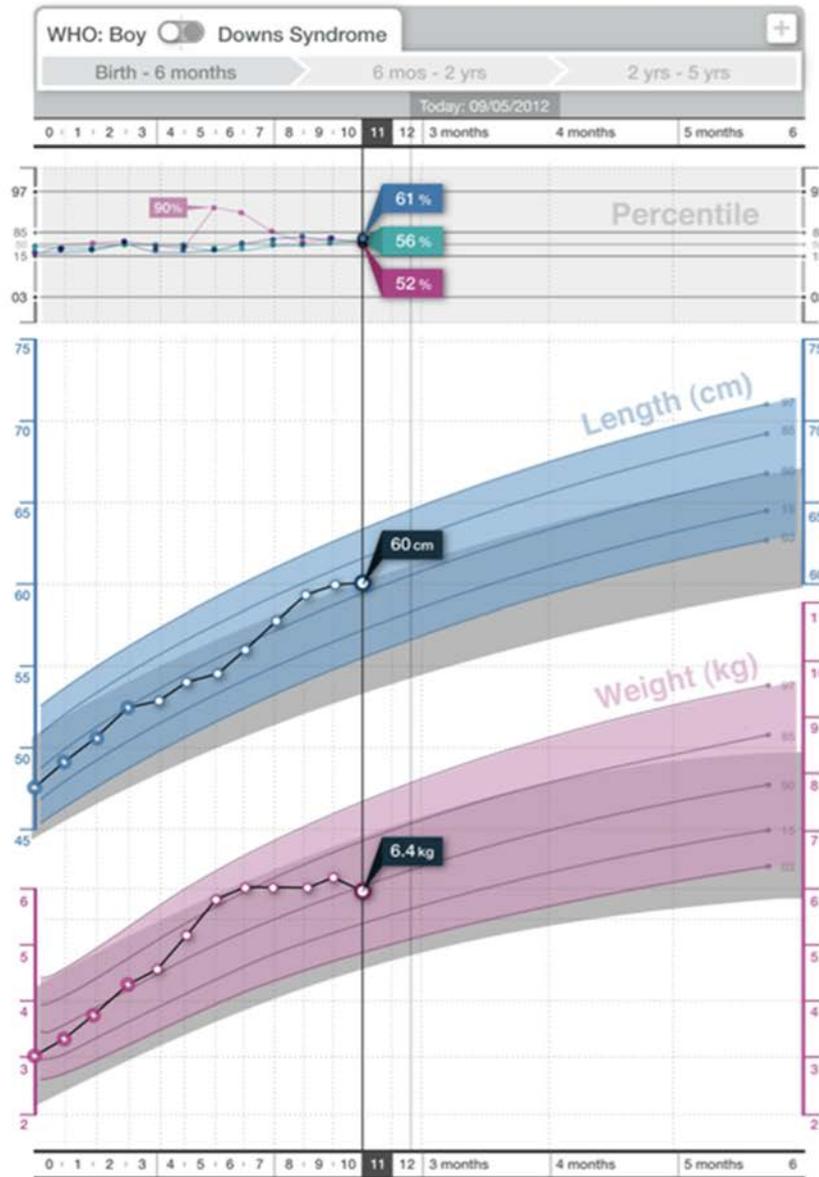
Desayuno	Almuerzo	Comida	Al acostarse
1			

Tome una (1) pastilla cada vez.
Take one (1) pill each time.

Instrucciones
Trague el medicamento sin aplastarlo o masticarlo.
Este medicamento se puede tomar con o sin alimentos.



SMART BP Centiles App Running on Cerner



Trial Eligibility



Female Male

43 y

Boston, MA

rheumatoid arthritis +methotrexate

Cancel

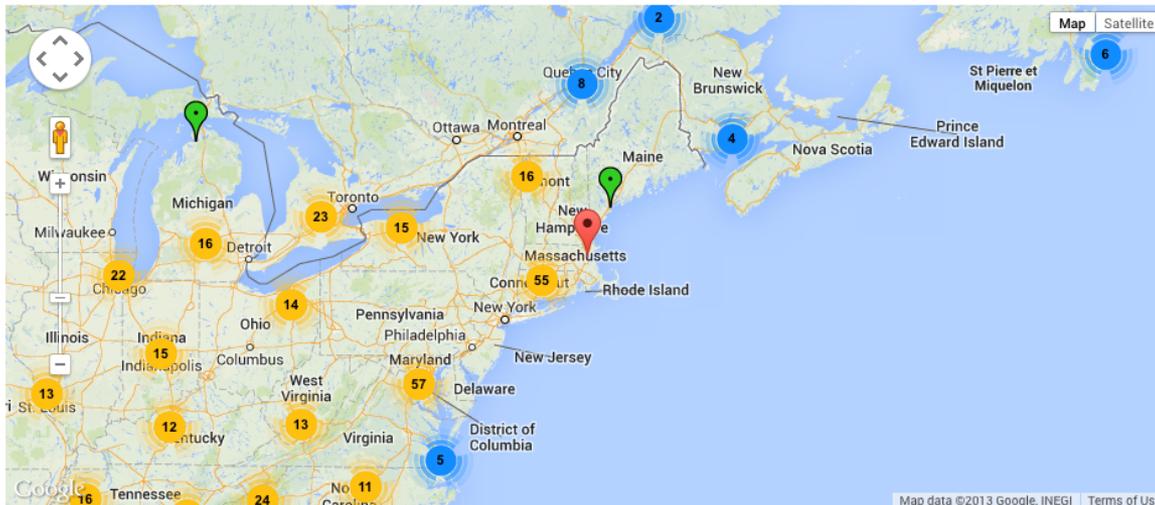
Refresh

Intervention / Observation

- Biological (14)**
- Device (1)
- Dietary Supplement (1)
- Drug (69)**
- Observational (14)
- Other (4)
- Procedure (1)

Trial phase

- N/A (8)**
- Phase 1 (8)**
- Phase 2 (23)**
- Phase 3 (17)**
- Phase 4 (26)**



Personalization of Therapy

**** Associate Attending(s) ****

**** No Known Allergies ****

BSA: 1.79 m2

Age: 18 years

Weight for Calc: 64.7 kg [07/24/2012]

DOB: 9/28/1993

Sex: Male

Outpatient [08/01/2012 13:02 - 08/01/2012 23:59]

Find: Starts with Type: Prescriptions

Folder:

- mercaptapurine 10 mg/mL oral Liq (compo
- mercaptapurine 50 mg oral tablet**

Discern:

Patient with TPMT Deficiency

DRISCOLL, ALEXANDER has a documented problem of TPMT - Thiopurine methyltransferase deficiency. Thiopurine methyltransferase (TPMT) is the enzyme responsible for the metabolism of mercaptopurine. Patients with TPMT - Thiopurine methyltransferase deficiency MAY require REDUCED doses of mercaptopurine.

Please page the Pharmacogenomics Service (pager #7454) if further information is required.

Alert Action

- Cancel order
- Acknowledge and override
- Modify**

History

Big Data Mashups: e.g., Personalized Medicine

- Linkage to external decision support services
- Pharmacogenomic rule sets
- Decision support for doctors

SMART Genomics Advisor

Robinson, William
DOB 1965-08-09 AGE 47 SEX M

Genomics Data

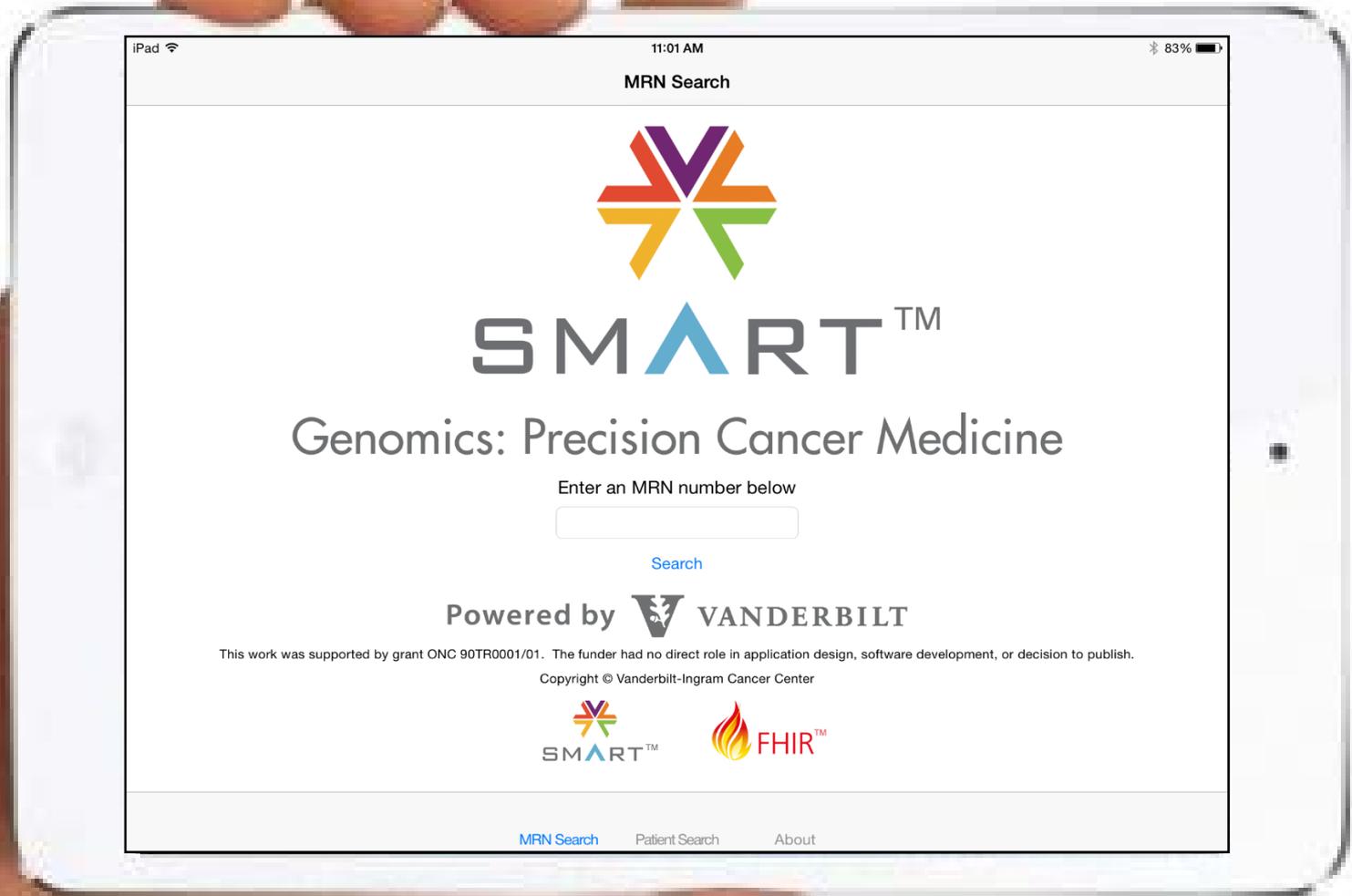
SNP	Locus	CHRM	Code	Risk	Frequency
Type 1 Diabetes					
rs7202877	16Q23	16	TT	0.95	81.0%
rs5753037	22Q12	22	CC	0.93	37.2%
rs3087243	CTL4A	2	AG	0.98	49.4%
rs3825932	CTSH	15	CT	0.94	43.4%
rs1990780	IFIH1	2	TT	1.16	36.2%
rs6822844	IL2	4	GT	0.73	30.2%
rs3184504	SH2B3	12	CC	0.74	26.0%
Total Relative Risk: 0.51					
Type 2 Diabetes					
rs2877716	ADCY5	3	CC	1.05	59.3%
rs2383208	CDKN2A	9	AG	0.88	28.2%
rs4402960	IGF2BP2	3	GG	0.92	46.2%
rs2237892	KCNO1	11	CC	1.03	86.5%
rs2793831	NOTCH2	1	TT	0.97	79.9%
rs7578597	THADA	2	TT	1.03	81.4%
rs7961581	TSPAN8	12	TT	0.95	53.4%
Total Relative Risk: 0.83					
Hypertension					
rs12413409	CYP17A1	10	GG	1.03	82.8%
rs17367504	MTHFR	1	AA	1.03	74.0%
rs3184504	SH2B3	12	CC	0.93	28.1%
Total Relative Risk: 0.99					
Coronary Heart Disease					
rs1746048	CXCL12	10	CC	1.05	70.6%
rs3184504	SH2B3	12	CC	0.89	30.2%
rs6725887	WDR12	2	TT	0.95	74.0%
Total Relative Risk: 0.89					

Disease Information

Patient is not at increased genomic risk for any Diabetes related comorbidities

Drug Advice

SNP	Genotype	Advice
rs20455	AA	Patients with the AA genotype who are treated with statins may have a decreased, but not absent, risk for adverse cardiovascular events as compare to patients with the AG or GG genotype. Other genetic and clinical factors may also influence a patients risk for adverse cardiovascular events.
rs2306283	AA	is not associated with decreased plasma AUC of pravastatin.
rs4149056	TT	A person with this genotype may have no increased risk of simvastatin-related myopathy.

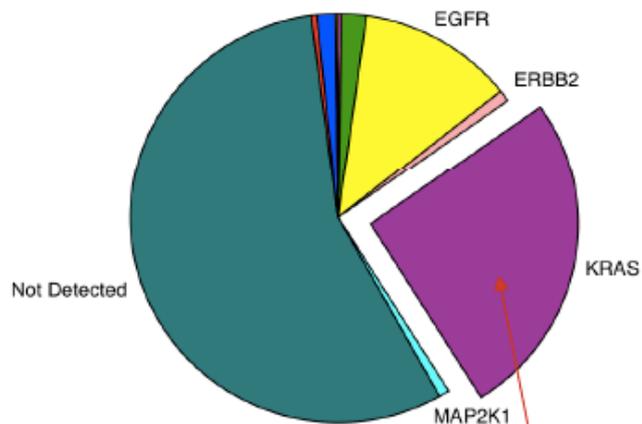


< Patient Search

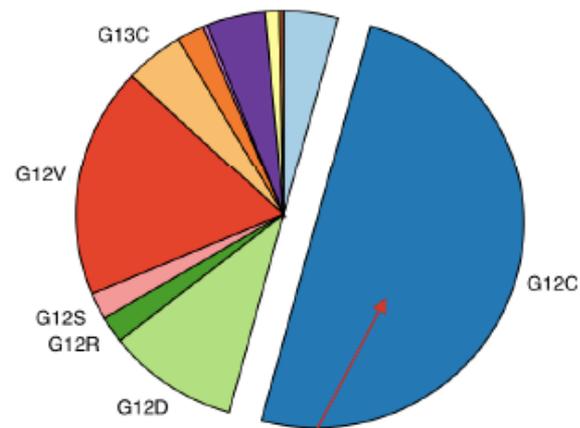
[Redacted] (MRN: [Redacted])

Male, [Redacted]
Diagnosis: Lung Cancer
Mutation: KRAS G12C

Mutated Genes Observed in Lung Cancer

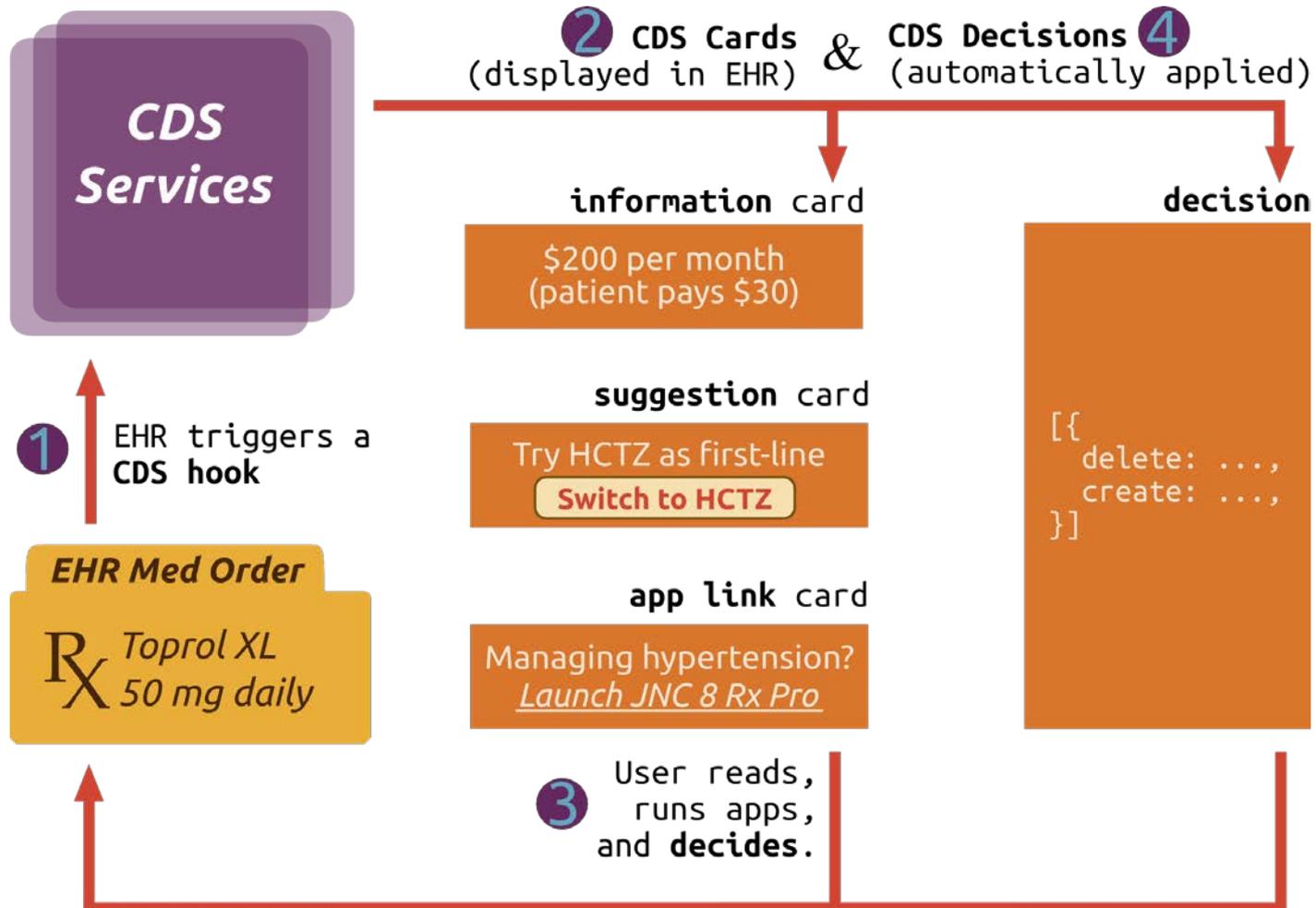


Observed Variants in Lung Cancer Patients with KRAS Mutation



A gene mutation was detected in this patient, so variant level information is also provided. They have the most common variant of KRAS seen in the *lung cancer* population.

CDS Hooks



Decision support integration e.g., immunization forecasting

< Amy Shaw >

Neelima Karipineni · Logout



Immunization Record SMART Application



Immunizations **References**

Child Adult Administered Due Recommended Not Recommended Optional

Amy Shaw (female, DOB: 2007-03-20)

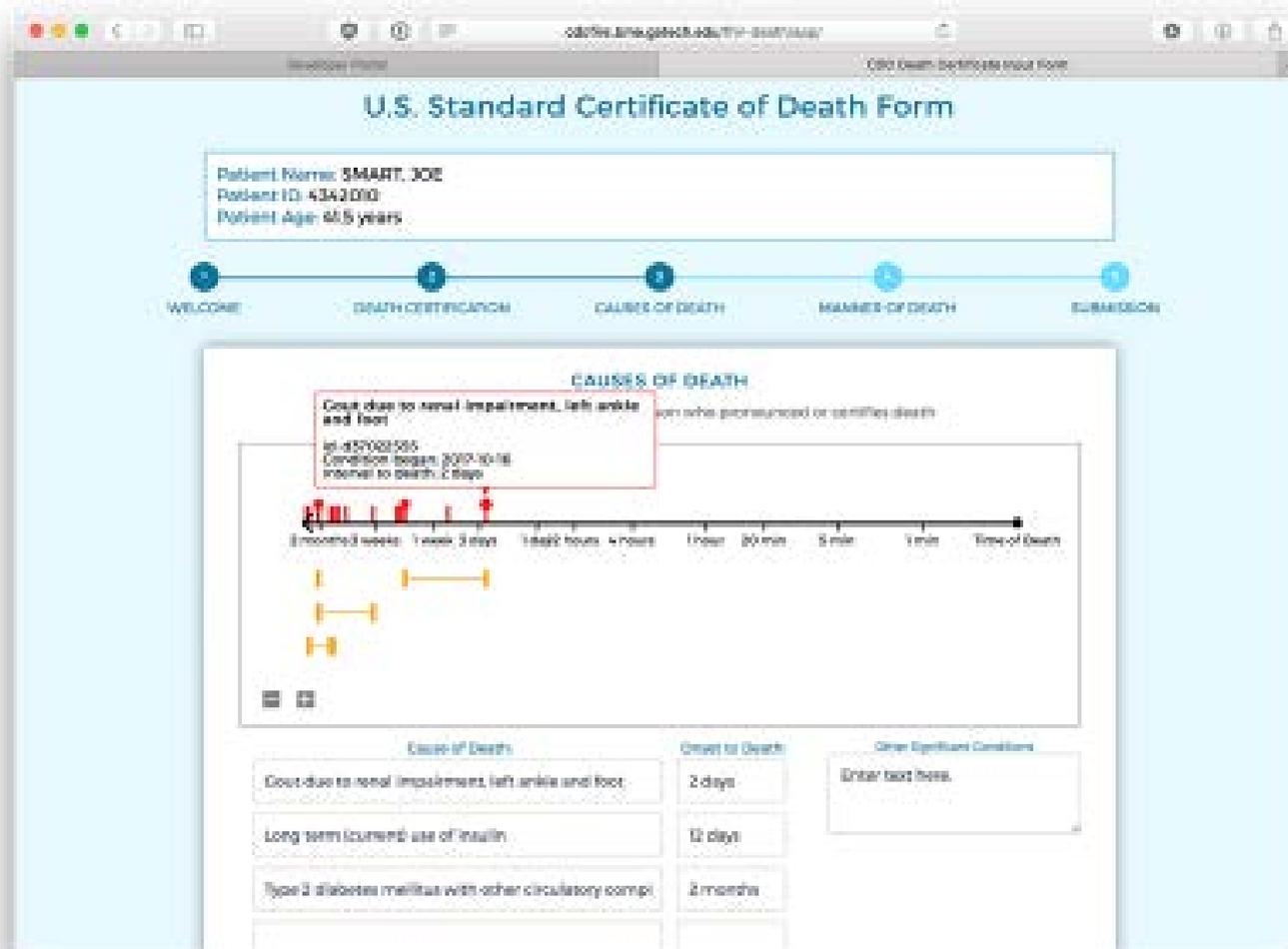
[Show Allergies](#)

Vaccine	Due	Doses			
ROTAVIRUS	5/1/12	5/24/07			
DTAP	3/1/12	9/27/07			
HepB	1/2/12 - 2/1/12	9/27/07			
POLIO	3/1/12	9/27/07	1/27/11	5/27/11	
HPV	1/1/23 - 1/1/24				
MENING	1/1/23 - 1/1/24				
HepA	1/1/13 - 7/1/13				
ZOSTER	Not indicated - Patient not yet indicated for ZOSTER vaccine				
VARICELLA	1/1/13 - 4/1/13				
HIB	3/1/12				
MMR	1/1/13 - 4/1/13				
PneumoPCV	3/1/12 - 4/1/12				
FLU	Not indicated - Current date is not within influenza season				

- Patient List
- Alerts
- API Playground
- API Verifier
- BP Centiles
- Direct Messages
- EMR View (Dev)
- Med List
- My App
- Problems
- Manage Apps

Vital Statistics

App Interface Design



http://apps.smarthealthit.org: The US Official App Store for Health

SMART® App Gallery BETA

Add New Listing Your Listings

Search



Login

Featured Apps

Featured Apps

Care Coordination

Clinical Research

Data Visualization

Disease Management

Genomics

Medication

Patient Engagement

Population Health

Risk Calculation

FHIR Tools



Adherence - Surescripts Medication Management Solution

Surescripts, LLC

Improves patient medication management via patient-specific insights, health plan-generated messages, and streamlined physician feedback.

View

Support: Web Designed for: Clinicians & Patients



Aggregated Patient Data

1upHealth

Helps providers view patient data aggregated from external health systems. Patients can connect their medical data sources using FHIR.

View

Support: Web Specialties: Trauma Designed for: Clinicians & Patients



Bilirubin Chart

Intermountain Healthcare

Demonstration app designed to help clinicians treat newborn hyperbilirubinemia appropriately.

View

Support: Web Specialties: Pediatrics Designed for: Clinicians



BP Centiles v1 (Open Source)

Boston Children's Hospital

Calculate a child's blood pressure percentiles, normalized by age, sex, and height

View

Perfect Storm for SMART Adoption

- EHR Vendors have implemented the SMART API
- Health systems standardizing on SMART
- MU3 Policy requiring API for patients
- Vendor implementation of S4S—patient access
- ONC/CMS Imprimatur and \$ for Gallery
- CDS Hooks Decision Support in Argonaut Process for implementation in EMRs
- SMART Genomics (PMI)

21st Century Cures Act



Real World Data

(a) IN GENERAL.—The Secretary shall establish a program to evaluate the potential use of real world evidence—

“(1) to help to support the approval of a new indication for a drug approved under section 505(c); and

“(2) to help to support or satisfy postapproval study requirements.

“(b) REAL WORLD EVIDENCE DEFINED.—In this section, the term ‘real world evidence’ means data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than randomized clinical trials.



The NEW ENGLAND JOURNAL of MEDICINE

A 21st-Century Health IT System — Creating a Real-World Information Economy

Kenneth D. Mandl, M.D., M.P.H., and Isaac S. Kohane, M.D., M.P.H.

Data generated as a by-product of the day-to-day work of delivery systems are a fundamental currency of the 21st Century Cures Act. How efficiently

of real-world evidence to advance treatment and research.

Fortunately, lawmakers included in the 21st Century Cures Act a provision that could transform

contains hundreds of thousands of apps because developers have a well-documented API that enables them to create software that seamlessly integrates with the op-



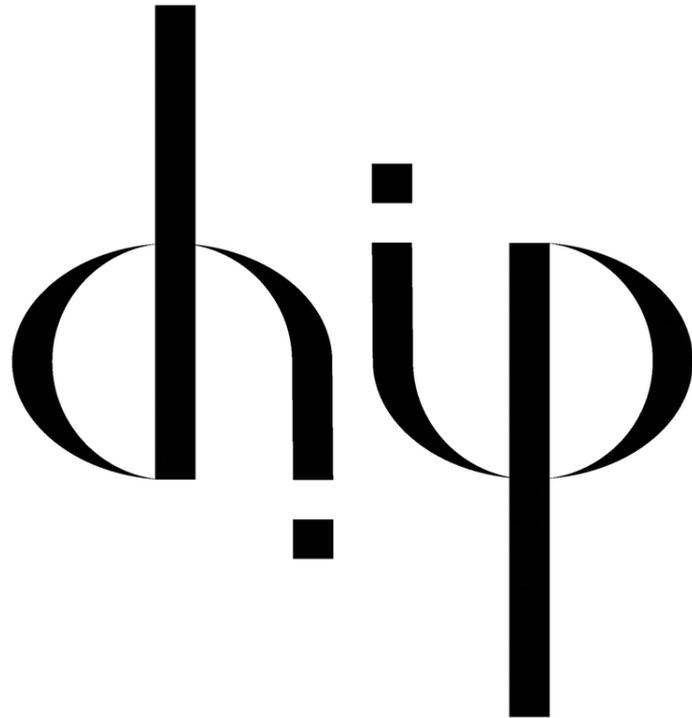
Public Health Opportunities

- Implementing guidelines as point of care decision support
- Capturing data at the point of care (case reporting)
- Exposing geographically-based data resources
- Contextualizing a patient's information with large datasets



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