Electronic Medical Records and Genomics: Possibilities, Realities, Ethical Issues to Consider

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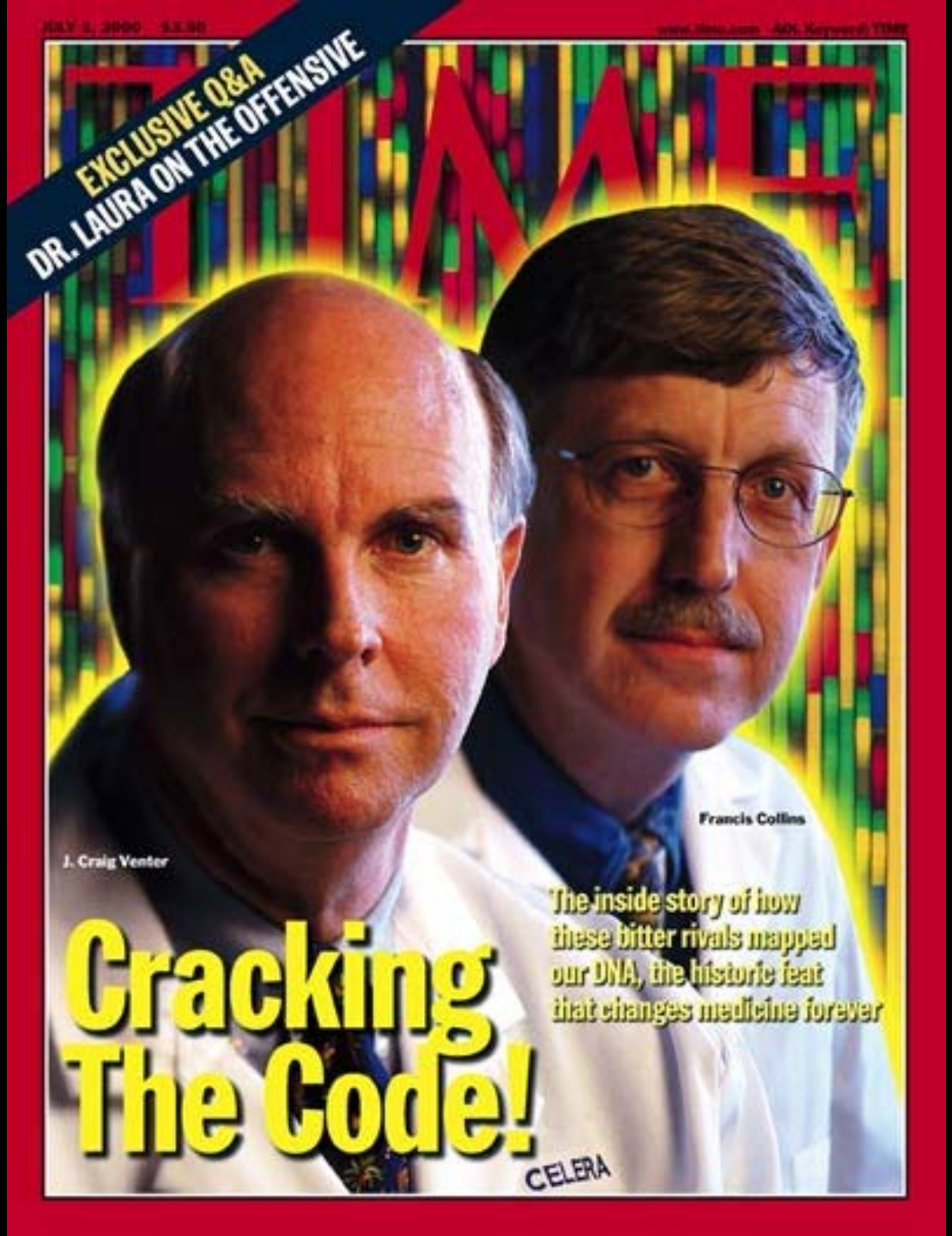
Possibilities:
the world of personalized health and healthcare



The Human Genome Project:

Draft sequence completed 2000

$3,000,000,000
15 years

The Vision

- Molecular and clinical biomarkers for health conditions individuals either have or are susceptible to
  - Includes traditional healthcare history, physical findings, diagnostic imaging, standard clinical laboratories
  - Increasingly: large volumes of molecular data
    - Structural genomics: DNA in residence (~22,000 genes)
    - Functional genomics: genes switched on (1-2% active)
    - Proteomics (400,000 proteins from 22,000 genes)

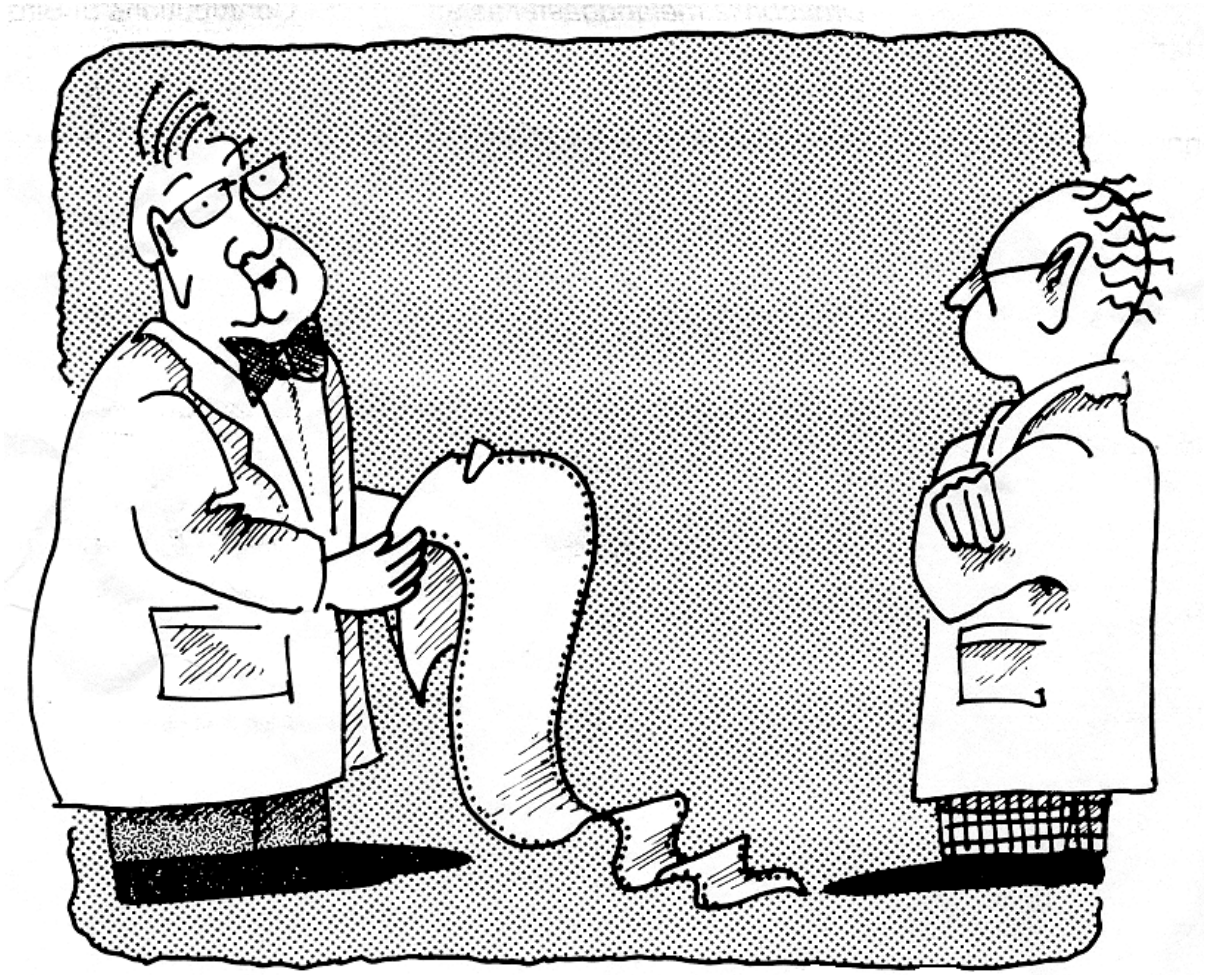
The Vision, cont'd

- Pharmacogenomics
  - "The right dose of the right drug for the right patient at the right time"
  - Drug development:
    - Avoid drugs likely to cause side effects
    - Re-investigate "back-burner" drugs
    - Develop entirely new drugs targeting fundamental disease processes

"Here's my sequence..."

New Yorker, 2000

The Genome Sequence is at hand…so?



"The good news is that we have the human genome.
The bad news is it's just a parts list"

Google
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Company announces low-cost DNA decoding machine

Updated 1/11/2012 9:13 AM

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NEW YORK – A biotechnology company announced it has developed a machine to decode a person's DNA in a day for $1,000, a long-sought price goal for making a person's genome useful for medical care.

PR NEWSWIRE

Life Technologies Corp. said Tuesday it was taking orders for the technology, which it expects to deliver in about a year. The Carlsbad, Calif., company said three major research institutions had already signed up for the $149,000 machine: the Baylor College of Medicine, the Yale School of Medicine and the Broad Institute of Cambridge, Mass.

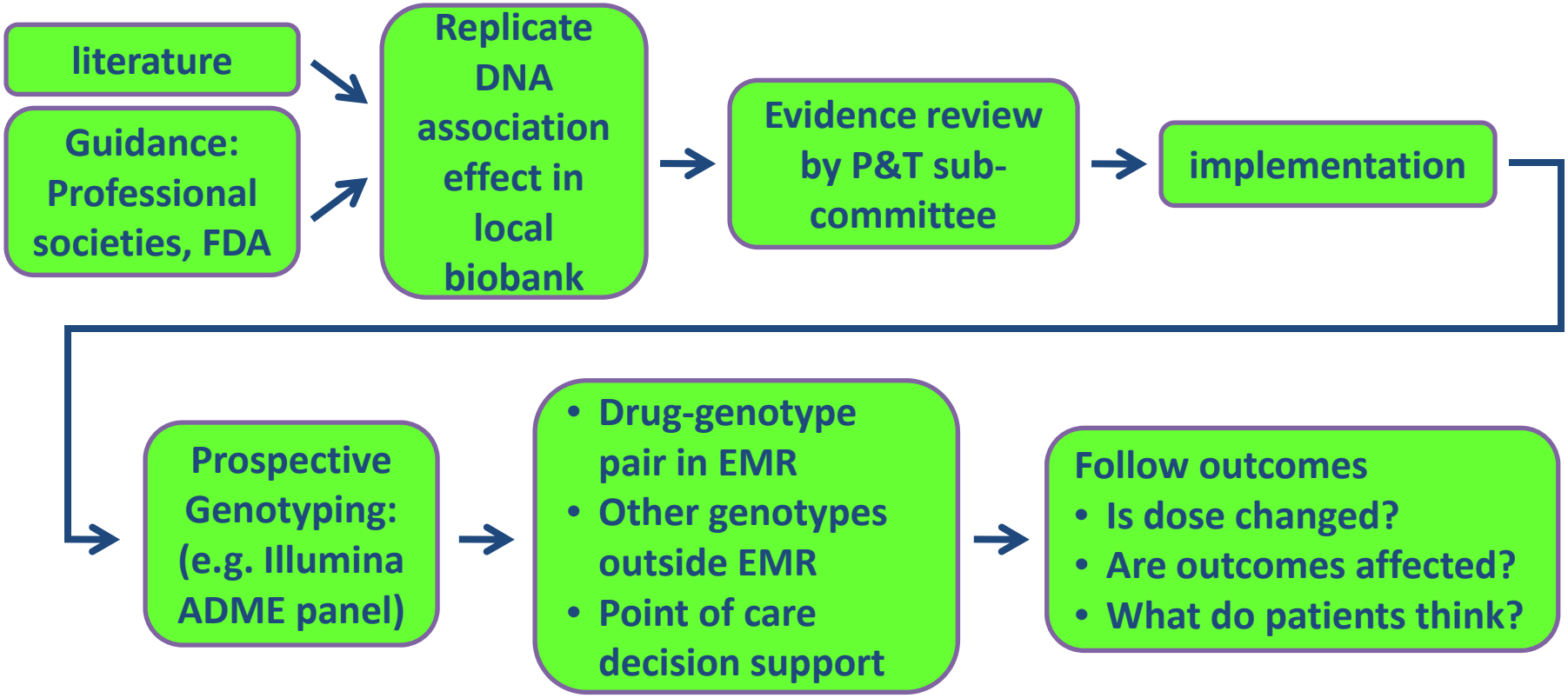
The machine is a sequencer, meaning that it lets scientists identify the sequence of the 3 billion chemical building blocks that make up a person's DNA. Since the

Realities - 2012

Electronic Medical Records have already proven themselves to be a ***essential bidirectional channel*** for DNA-enabled healthcare and for advancing health sciences

Example of current operational "genomic EMR" system: Vanderbilt PREDICT project

Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment.
Go-live date: September 2010



As seen by providers at the moment of prescribing:

HEO Popup

Clopidogrel Poor Metabolizer Rules

Genetic testing has been performed and indicates this patient is at risk for inadequate anti-platelet response to clopidogrel (Plavix) therapy

This patient has been tested for CYP2C19 variants, and the presence of the ***2/*2** genotype has identified this patient as a **poor metabolizer** of clopidogrel. Poor metabolizers treated with clopidogrel at normal doses exhibit higher rates of stent thrombosis/other cardiovascular events.

Treatment modification is recommended:

- ○ Prescribe prasugrel (EFFIENT) 10mg daily and stop clopidogrel (PLAVIX) startdate, 10 AM

Due to increased risk of bleeding, prasugrel should not be given to patients:

- that have a history of stroke or transient ischemic attack ***** Not known; please check StarPanel**
- that are greater than 75 years of age
- whose body weight is less than 60 kg

Click here for **more information**

If prasugrel (EFFIENT) not selected, please choose desired action:

- ◉ Increase maintenance dose of clopidogrel (PLAVIX) 150 mg daily, startdate, 10AM
- ○ Maintain requested daily dose of clopidogrel (PLAVIX) 75 mg daily, startdate, 10AM

- ○ Contraindicated
- ○ Expected effects (e.g. nuisance bleeding)
- ○ Patient preference
- ○ Other

Click here for **more information**

Cancel | Order

NOTE: The Vanderbilt P&T Committee has recommended that prasugrel (if not contraindicated) should replace clopidogrel for poor metabolizers; if this is not possible consider doubling the standard dose of clopidogrel (or, use standard dose clopidogrel). However, there is not a national consensus on drug/dose guidance in this population.

Back | Home | Close

Electronic Medical Record genomic data as viewed by providers

Alert **Clinical Trial Participant** Actions

StarTracker Conditions/Diseases: No Tracked Conditions ♦Customize

**** notation indicates test is due for repeat and value may be outdated.*

Preventive	BP	BMI	eGFR	HCT	FLUVAX	CRC	Mammogram	PAP
	143/72	31.7 (12/30/2010)	52	33	NONE	NONE	UNKNOWN	UNKNOWN
	SMOKE							
	UNKNOWN							

Patient-specific guidelines MedicationsLog ICD9 History **Update** **Update (free text)** NoChang

General Information:

PCP:

Primary cardiologist:

Significant Medical Diagnoses and Conditions:

1. Coronary atherosclerotic heart disease
a. NonSTMI 01/2010
b. Coronary intervention 1/12/2010
(1) Xience 3x23 drug eluting stent to RCA
c. Coronary intervention 2/17/2010
(1) two 2.5x28 and 2.25x18 Cypher DES to LAD and diagonal
d. Coronary intervention 4/6/2010

Adverse and Allergic Drug Reactions:
penicillin (class) (rash)
cephalexin (rash)

Drug Genome Interactions: *(12/21/10 08:02)*
clopidogrel sensitivity: POOR METABOLIZER, REDUCED ANTI-PLATELET EFFECT - gene: CYP2C19 - gene result: *2/*2

Medications: prepare to print print and give pt. Show Hx of medications
Drug/Herb Interactions
aspirin 325 mg orally once daily, in the morning
prasugrel (effient) 10 mg orally once daily
carvedilol 6.25 mg orally twice daily with meals
lisinopril 10 mg orally once daily
furosemide 40 mg orally once daily

Genomic data as viewed by patients

My Health At Vanderbilt Hom...

VanderbiltHealth.com: For Patients and Visitors

You are currently logged into MyHealthAtVanderbilt

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My Health *at* Vanderbilt

Help: Using MyHealth

Home Page For: QAPATIENTE, GREEN beth.dunaway@vanderbilt.edu

All Health Topics

- View all Health Topics

Alzheimer's Disease

- What is Alzheimer's Disease?
- Alzheimer's Caregivers
- Understanding Asthma

[more stories]

Be Healthy, Stay Healthy

- Abdominal Aortic Aneurysm Screening
- Blood Pressure Screening
- Breast Cancer Screening

[more stories]

Health News You Can Use

- Safety Experts at Monroe Carell Jr. Childrens Hospital at Vanderbilt Warn Parents and Caregivers Against the Dangers Associated with Drop-Side Cribs
- Five Holiday Resolutions for Cancer

Account Access

- View others who have access to QAPATIENTE, GREEN

Messaging

- Message Your Doctor's Office

Clinical Record

- View Your Clinical Record
- Genes that affect my medicines

Appointments

Request an appointment with

- Your Doctor
- New Doctor
- View Existing Appointments

Health Screenings

- Peripheral Artery Disease--are you at risk?

Research Opportunities

- Interested in participating in research studies? Join ResearchMatch now!
- Search currently enrolling clinical studies

Patient Resources

- Vanderbilt Giving
- Information about a

My Health At Vanderbilt Gene...

VanderbiltHealth.com: For Patients and Visitors

You are currently logged into MyHealthAtVanderbilt

Log Out Here

My Health *at* Vanderbilt

Help: Using MyHealth

Home | Account Access | Messaging | Clinical Record | Appointments | Billing | Account Maintenance

Genes that affect my medicines QAPATIENTE, GREEN

beth.dunaway@vanderbilt.edu

This test examines your gene known as CYP2C19 (sounds like "sip-2-C-19"). CYP2C19 can affect your response to a drug called clopidogrel (sounds like "kloh-PID-oh-grel"). Clopidogrel has the brand name Plavix. Clopidogrel is used to help prevent harmful blood clots from developing, such as for people who have had a recent heart attack, or a stroke.

CYP2C19 Results: Your result is *1/*2. This means you may not respond as well to clopidogrel.

Many factors, including this test, help your doctor decide if taking clopidogrel is right for you.

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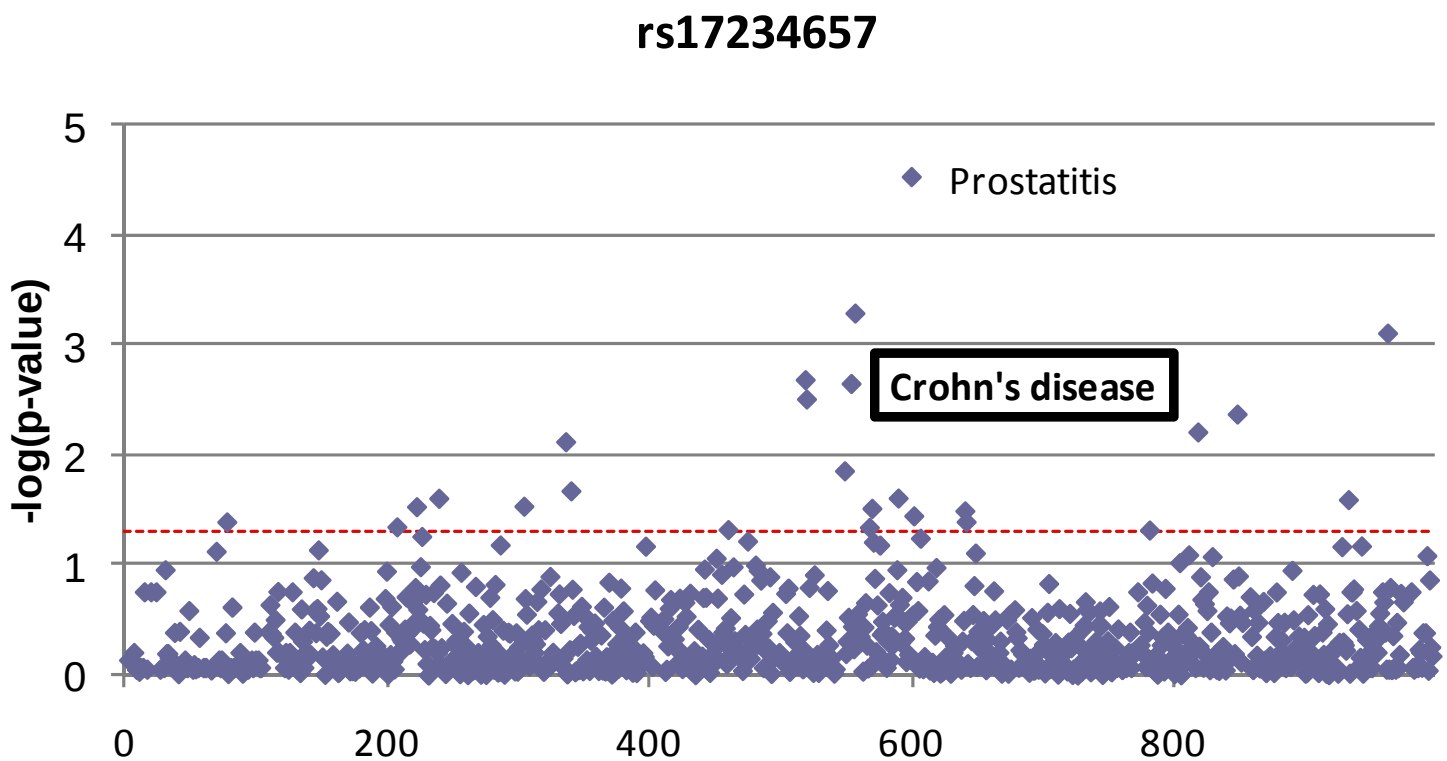
Version: 6.1.76_78492-int

EMR data is advancing genomic health science:
PheWAS: PHEnome Wide Association Studies

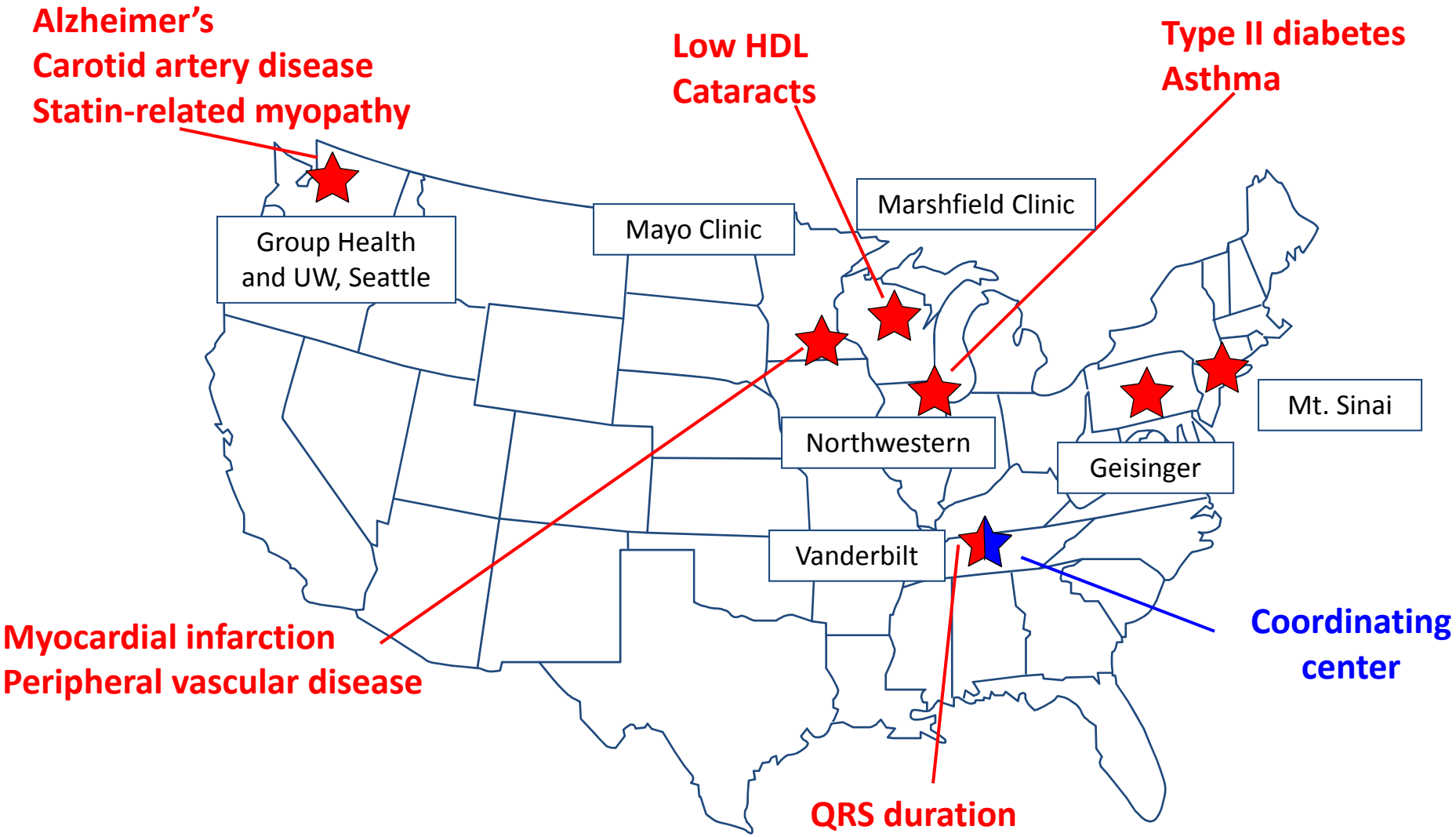
- GWAS: pick a phenotype → interrogate the set of all genetic polymorphisms for association
- PheWAS: pick a genotype → interrogate the set of all phenotypes (diseases) as recorded in EMR



The eMERGE Network

electronic Medical Records & Genomics

A consortium of biorepositories linked to electronic medical records data for conducting genomic studies



Realities of 2012

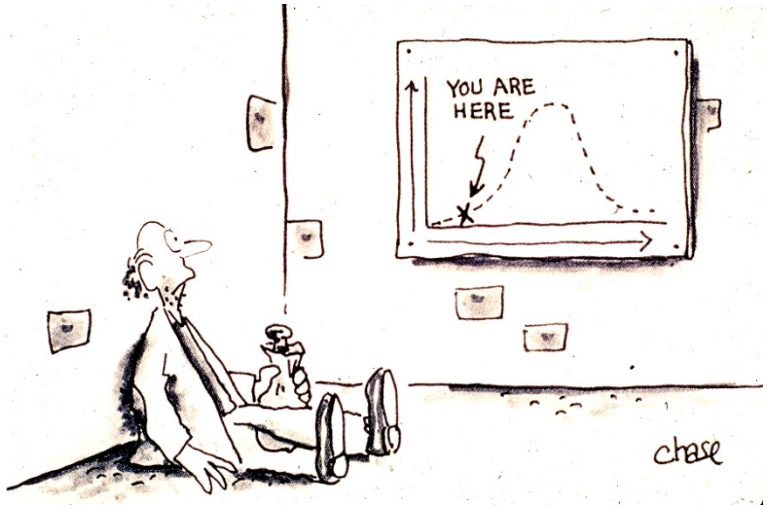
- Our ability to acquire person-specific DNA data far exceeds our understanding of its meaning
- Genetic data conclusively explains the basis for only a tiny set of the 8000+ diseases of humans and responses to therapy
- As a result DNA data acquired now will likely need to be re-interpreted many times over in the future as DNA science unfolds

General observations about clinical genomics

- Genomic data is the current poster child for complexity in healthcare
- No practitioner can absorb and remember more than a tiny fraction of the knowledge base of human variation
- Therefore, computerized clinical decision support is the only effective way to insert genomic variation-based guidance into clinical care

Current state of EMR and decision support infrastructure

- Only 1.5% of US hospitals have full adoption of a comprehensive EMR*
- Only 17% of hospitals have computerized provider order entry (point for decision support alerts and reminders)*

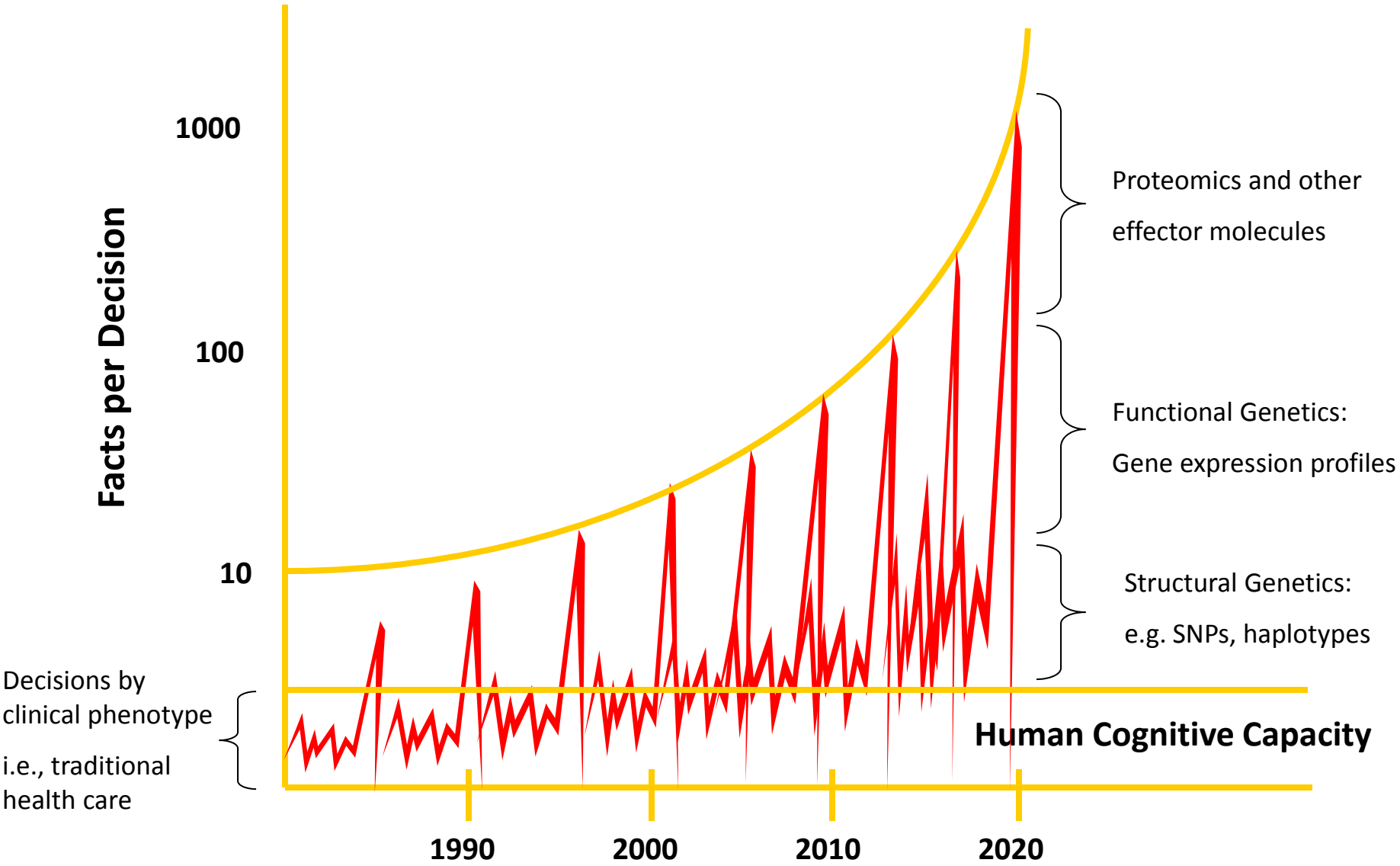


*Jha AK, Blumenthal D, et al. N Engl J Med. 2009 Apr 16;360(16):1628-38.

Issues to consider

1. Is it ethical to allow healthcare providers to continue to practice without a systems infrastructure for decision support?

The Need for Computerized Patient-Specific Decision Support



Issues to consider

1. Is it ethical to allow healthcare providers to continue to practice without a systems infrastructure for decision support?
2. Is it ethical to discard person-specific DNA data that currently has uncertain or unknown significance?

Most common current method for delivery of genotyping into clinical operations (discards DNA data obtained that has no demonstrated clinical relevance)

DEPARTMENT OF PATHOLOGY
Nashville, Tennessee 37232

Michael Laposata, M.D., Ph.D.
Medical Director, Diagnostic Laboratories
CLIA #44D0659066

Name:	Sex:	Laboratory Number:	VUH#:
[redacted]	F	[redacted]	[redacted]

Referral Source: Dr. Kim Ely

Reason for Request: DNA Analysis for *KRAS* Mutations

Type of Specimen: Paraffin-Embedded Tissue (Block #: [redacted])

Date Received: 2/12/10

Date of Report: 2/18/10

Interpretation: *KRAS* Mutation NOT Detected

Mutations Tested Include:
G12A, G12C, G12D, G12R, G12S, G12V, G13C, G13D

The *KRAS* gene (12p12) is a member of the Ras family of proto-oncogenes, and encodes a protein containing guanosine nucleotide triphosphate hydrolysis activity (known more commonly as a GTPase). These proteins are active when bound to guanosine triphosphate (GTP) and inactive when bound to guanosine diphosphate (GDP). *KRAS* is membrane bound, is activated by growth factor receptors, and through BRAF, stimulates the MAPK/ERK pathway resulting in transcription and cell proliferation. *KRAS* mutations are observed in colon cancer (40-50%), lung cancer (20-30%) and pancreatic cancers (90%). Conserved missense mutations in codons 12 and 13 result in prolonged binding of GTP and constitutive activation of RAS proteins, thereby leading to uncontrolled cell proliferation.

Progressive and/or metastatic non-small cell lung adenocarcinomas are often treated with inhibitors of the EGFR receptor as a second line therapy. However, it has been shown that tumors, which harbor mutations in codons

Issues to consider

1. Is it ethical to allow healthcare providers to continue to practice without a systems infrastructure for decision support?
2. Is it ethical to discard person-specific DNA data that currently has uncertain or unknown significance?
3. How does ‘genomic consent’ differ from standard consent for healthcare services?

How do terms of consent change…

- When a person lacks basic ‘genetic health literacy’?
- When a health condition does not currently exist but may in the future?
  - Treatable vs. (currently) non-treatable conditions
- When a health condition has implications only for one’s offspring, not self
  - And the literacy and health preferences of one’s heirs is different than one’s own
- For incidental findings vs. disease-specific testing?