

Tales of Tenerife and Three Mile Island: Lessons from Other Industries for Genomic Clinical Decision Support

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Genomic Clinical Decision Support
Developing Solutions for Clinical
and Research Implementation
October 2, 2014

Keynote Talk Tips #1 and #2

1. Know your audience



2. Shorter is better

Marc Williams, MD
Personal communication
Sept. 29, 2014

Topics

- The nature of genomic data
- Lessons from other industries about managing complexity
- Elements of an 'ideal state' for genomic clinical decision support
 - Data representation
 - Knowledge management
 - Implementation

The nature of 'omics data in a clinical context

- Voluminous (billions of base pairs per genome, hundreds of thousands of proteins, tens of thousands of genes, thousands of expression levels)
- Single nucleotides matter. E.g., sickle cell disease
- No perfect laboratory methods at present; all generate data with blind spots and errors
- Only a small fraction of total observable data conclusively associated with health status at present
- Molecular control mechanisms poorly understood
- Interpretation of molecular variation is changing rapidly



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Technical desiderata for the integration of genomic data into Electronic Health Records

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ARTICLE INFO

ABSTRACT

Output of workshop on “Integration of Genetic Test Results into Electronic Medical Records” convened by the National Heart Lung and Blood Institute, Bethesda, MD August 2-3, 2011

7 desiderata for genomic sequence data in EHRs

1. Lossless data compression from (high volume) primary observations to clinically relevant subsets.
2. Since methods will change, molecular lab results carry observation methods with them (LOINC model)
3. Compact representation of clinically actionable subsets for optimal performance (clinician thinkspeed = 250msec)
4. Simultaneously support for human-viewable formats (with links to interpretation) and formats interpretable by decision support rules.
5. Separate primary sequence data (remain true if accurate) from clinical interpretations of them (will change with rapidly changing science)
6. Anticipate the boundless creativity of Nature: multiple somatic genomes, multiple germline genomes for each individual over their lifetime.
7. Support both individual care and discovery science



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Commentary

Technical desiderata for the integration of genomic data with clinical decision support

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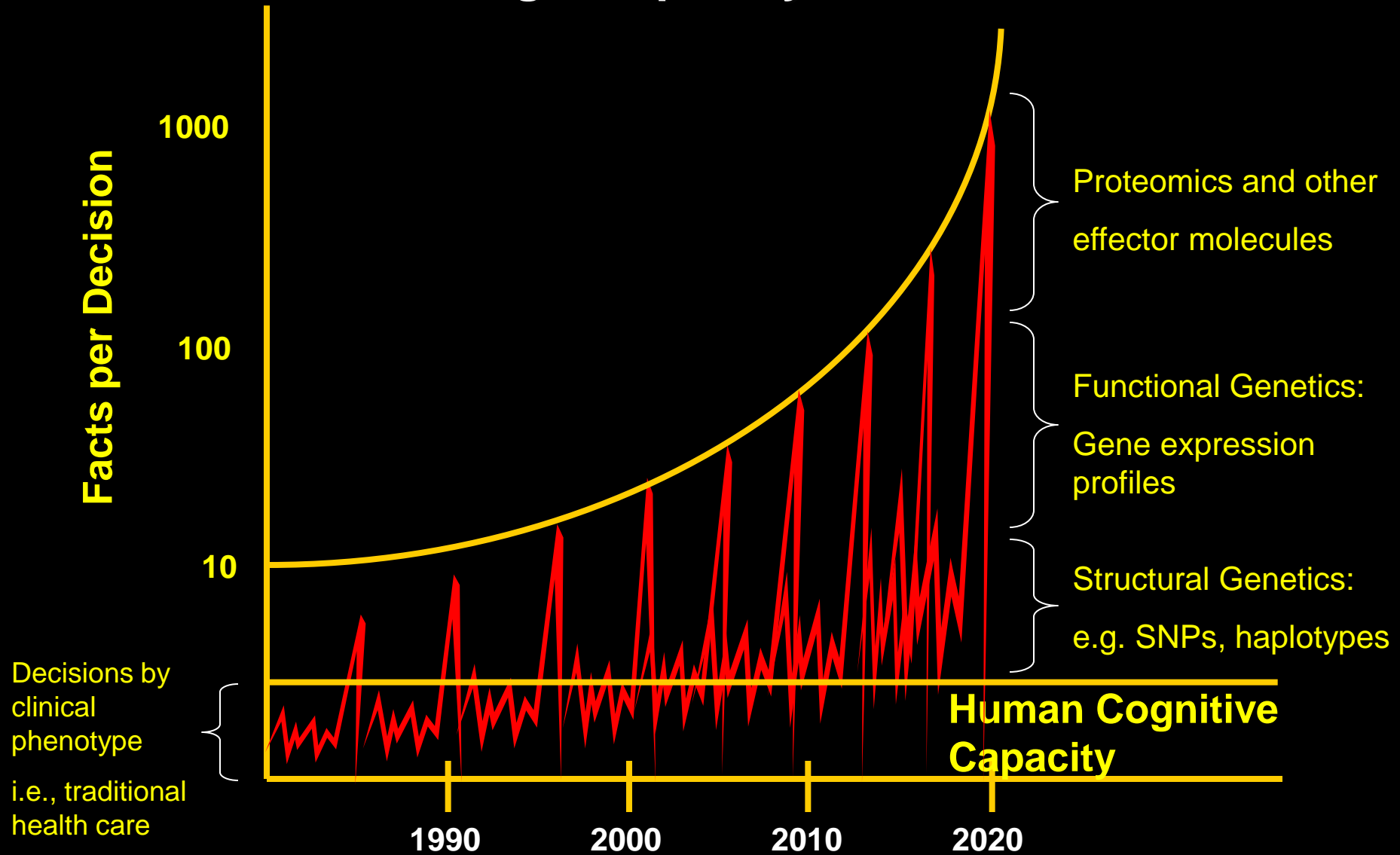
ABSTRACT

The ease with which whole genome sequence (WGS) information can be obtained is rapidly approaching the point where it can become useful for routine clinical care. However, significant barriers will inhibit

Additional desiderata for the technical integration of whole genome sequences (WGS) with Clinical Decision Support (CDS)

8. CDS knowledge must have the potential to incorporate multiple genes and clinical information
9. Keep CDS knowledge separate from variant classification
10. CDS knowledge must have the capacity to support multiple EHR platforms with various data representations with minimal modification
11. Support a large number of gene variants while simplifying the CDS knowledge to the extent possible
12. Leverage current and developing CDS and genomics standards
13. Support a CDS knowledge base deployed at and developed by multiple independent organizations
14. Access and transmit only the genomic information necessary for CDS

Molecular data driving escalating complexity in Healthcare



Keynote Talk Tip #3

Talk about what you really know

Personal experience adds credibility

Context for what follows



Association for the
Advancement of Medical
Instrumentation
workshop July 2012

AAMI MONOGRAPH

Risk and Reliability
In Healthcare and
Nuclear Power
Learning from Each Other

Edited by Matthew B. Weinger, MD,
Bruce P. Hallbert, PhD, and Mary K. Logan, JD



AAMI
Advancing Safety in Medical Technology

Similarities and differences among industries

Characteristic	Healthcare	Commercial Aviation	Nuclear Power
Serve a public good	++++	++++	++++
Highly trained professionals	++++	++++	++++
High hazard sociotechnical systems	++++	++++	++++
Highly regulated	++++	++++	++++
Methods and practices standardized	+	++++	++++
Rapid industry wide adoption of best practices	+	++++	++++ (historically ++)
Reliance on individual professionals acting autonomously	++++	+(historically +++)	+

Keynote Talk Tip #4

People like stories

(as long as they are brief and relevant)

Reliance on individual professionals acting autonomously

- The story of Captain Jacob Van Zanten

KLM. From the people who made punctuality possible.

Building an airline of KLM's standing requires a special kind of dedication. Like making a point of being punctual. A quality that's very much part of the Dutch.

It was Christiaan Huygens after all, who gave it real significance – when he invented the spring balance that made timepieces transportable. A creation without which life is inconceivable. Or air travel, for that matter. And one that illustrates that singular Dutch ability for doing things well. As you'll discover when you fly KLM. You'll find your trust sincerely reciprocated. With efficiency, punctuality and friendly understanding.

For that is the way the people of Holland are. People whose involvement make KLM a big, reliable, international airline. As your travel agent will confirm.



Visit any of Holland's clog-makers and watch Dutch craftsmanship and precision in the old tradition. In this time-honoured process, logs are split, hollowed, shaped, smoothed and ultimately transformed into the article still worn in many parts of the country.



A right royal time is what you have in KLM's Royal Class Service is punctual and princely. Dinner for instance, is always rounded off with a choice of seven different coffees. But then, it's only in keeping with that stylish class far too good to be called just first.

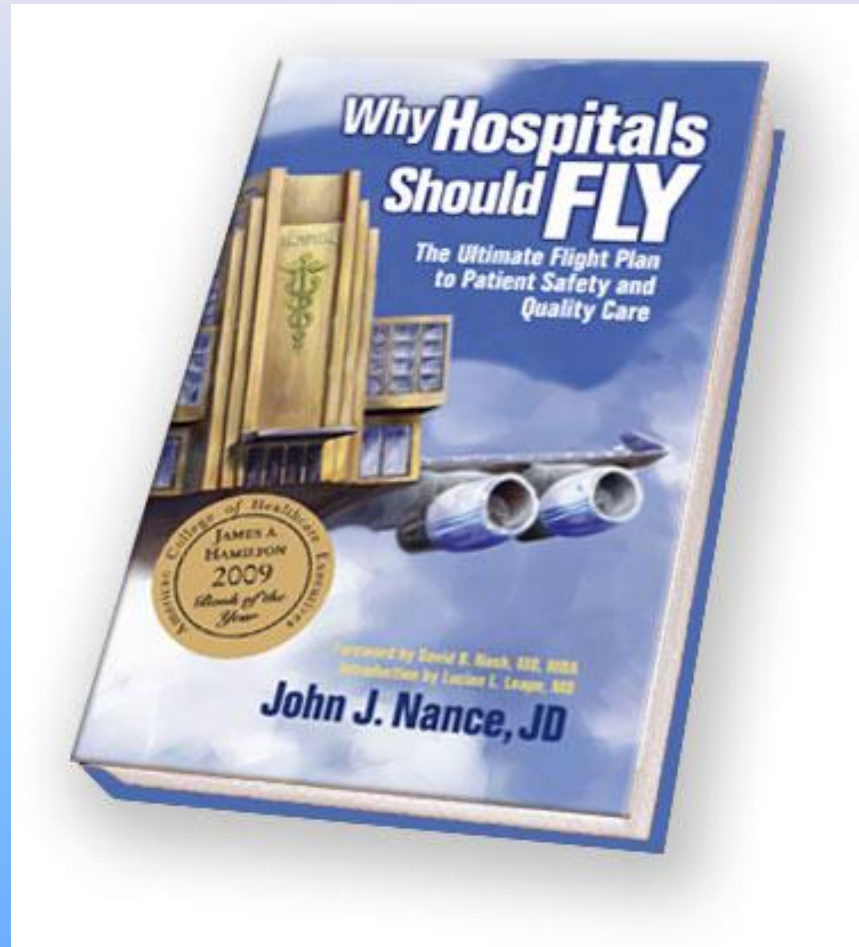


The reliable airline of those surprising Dutch.



Lesson: The Most Perfect Pilot (Chief Safety Officer) causes the worst aviation disaster in history. Aviation changes forever the model of reliance on autonomous individuals.

For the rest of the story...



Industry-wide problem solving and rapid adoption of best practices

- The story of Three Mile Island



“What happens to one of us happens to all of us”

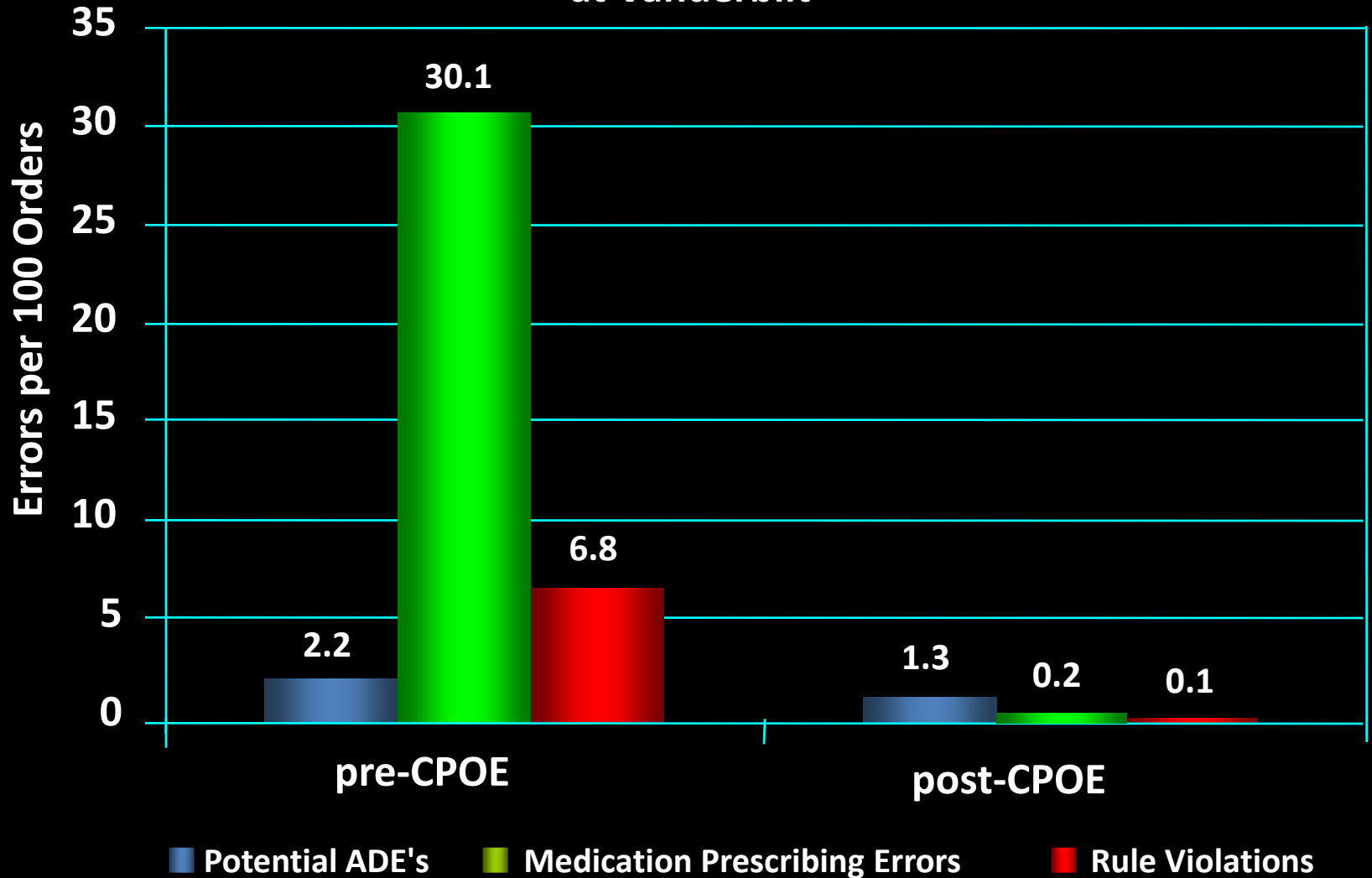
Keynote Talk Tip #5

It is better to light a candle
than curse the darkness

Chinese proverb

The promise of automated patient-specific
Clinical Decision Support (CDS)

Effect of Computerized Provider Order Entry (CPOE) with CDS at Vanderbilt



The scope of decision support

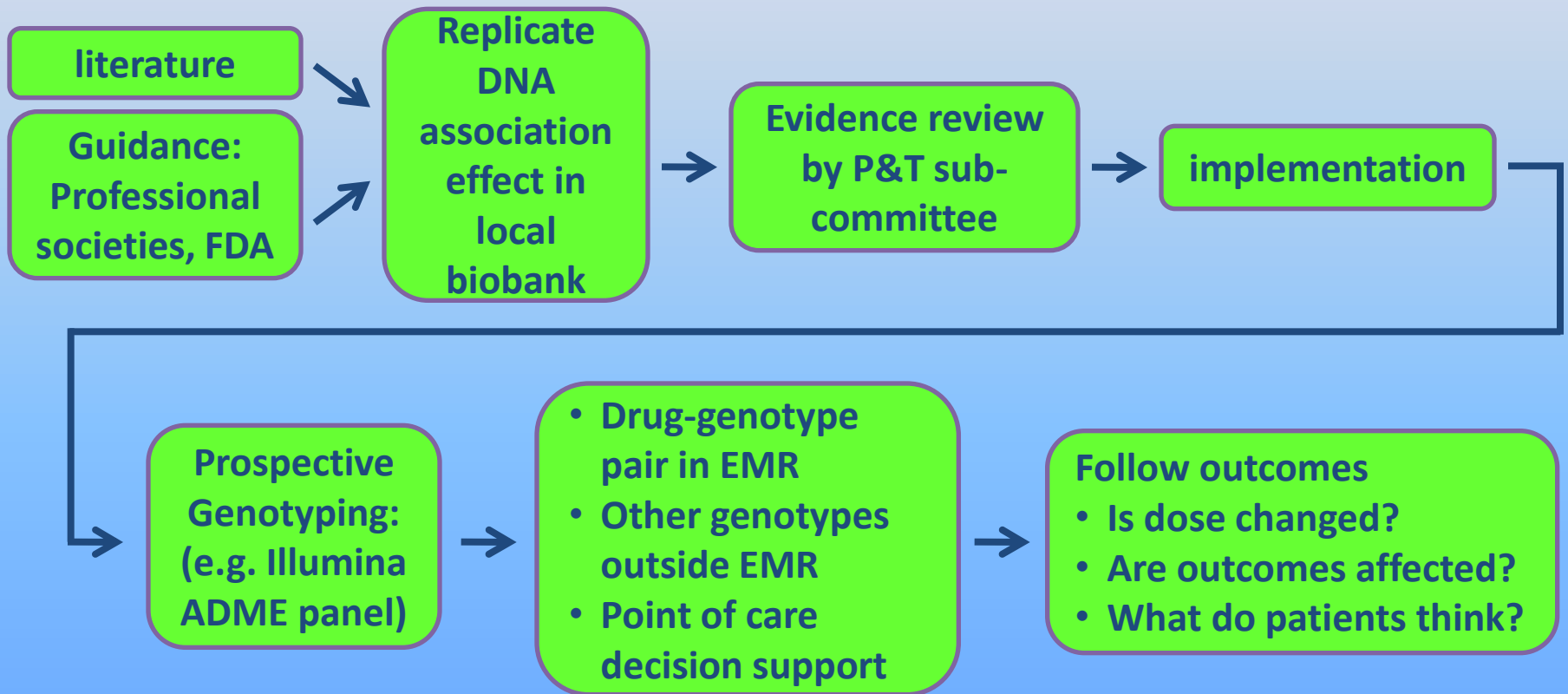
- “Rule based systems” do not mean providers must follow rules. Rules in informatics context = computerized approach to identification of characteristics.
- Examples of interventions
 - Educational prompts: here is additional general information to consider in this setting.
 - Data gathering prompts: given what is known about this {genotype | phenotype | genotype+phenotype}, it would be helpful to get this additional observation or testing.
 - Guidance that improves certainty of diagnosis given data currently available.
 - Guidance for best-evidence-based therapy selection
 - Information relevant to prevention and/or prognosis.

An example of progress towards
operational genomically enabled
decision support

Vanderbilt PREDICT project

Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment.

Go-live date: September 2010



Van Driest SL et al. Clinically actionable genotypes among 10,000 patients with preemptive pharmacogenomic testing. Clin Pharmacol Ther. 2014 Apr;95(4):423-31.

Example of patient-specific decision support 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](#)

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.

Key computer technology: event monitor

Elements of an 'ideal state' for genomic clinical decision support

Keynote Talk Tip #6

It is better to be approximately right
than precisely wrong

Samuel I. Rapaport, MD

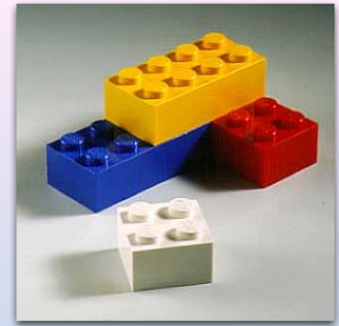
Genomic CDS “ideal state” as seen by users

- Always up to date
- Content can be (re)purposed for different types of users: specialist and nonspecialist health professionals, lay persons, families
- Health literacy and numeracy sensitive
- Explains all its actions and recommendations
- Adaptively learns what each user knows and doesn't know: appears to 'get smarter' with use (and actually does get smarter...)

Genomic CDS “ideal state” as seen by healthcare organizations

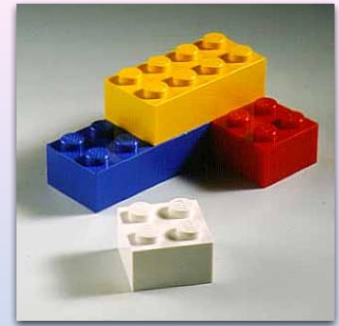
- A systems infrastructure to improve quality and consistency by autonomous individual providers and by healthcare teams
- Tracks decision support events, and provides basis for correlating subsequent clinical course with guidance provided, **whether or not** users followed the guidance.
- Contributes to local continuous process improvement and to a shared national ‘learning healthcare system.’

Building Blocks for an ideal CDS



- Knowledge Representation Standards for interoperable electronic “decision support packages” containing:
 1. Recognition logic for conditions of interest as represented in EHR systems (both genotype and phenotype)
 2. Guidance for target users (clinician, patient, family)
 3. Recognition logic for “closed loop decision support”: process or outcome measure to monitor, along with record of whether user accepted or rejected guidance

Building Blocks for an ideal CDS, cont'd



- Decision support authoring systems: tools to enable local clinicians to easily import, review, and implement decision support packages received from a Public Library of Decision Support packages
- Event monitors embedded in EHR and PHR systems
- System-generated alerts at the “teachable moment” of diagnostic testing, therapy decision making, counselling
- Automated tracking of outcomes vs. user decisions

The 'ideal' CDS Public Library

1. A CDS Information Commons based on the principle that “What Happens to One of Us Happens to All of Us”
2. Managed by a neutral, trusted organization (multiple possibilities)
 - National Library of Medicine
 - Clinical Decision Support Consortium
 - A Wikipedia-like .ORG

Implementation:

Closing the Loop nationally

- *Quid pro quo* for use of public library clinical decision support packages would be automated local monitoring whether guidance was accepted or rejected, and whether subsequent clinical events (phenotypes) occurred or did not occur.
- Local uploads to the Public Library of aggregate local outcomes -> a national Learning Healthcare System that learns from every decision support event, whether or not recommendations were accepted by clinicians.

Keynote Talk Last Tip

Any fool can know.
The point is to understand.

Albert Einstein