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

Daniel Masys, MD

Affiliate Professor

Biomedical & Health Informatics
University of Washington, Seattle

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

1. Know your audience

PREACHING TO THE CONVERTED?

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

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

Daniel R. Masys [a,*], Gail P. Jarvik [b,c], Neil F. Abernethy [a], Nicholas R. Anderson [a], George J. Papanicolaou [d], Dina N. Paltoo [e], Mark A. Hoffman [f], Isaac S. Kohane [g], Howard P. Levy [h]

[a] Division of Biomedical and Health Informatics, Department of Medical Education and Biomedical Informatics, University of Washington, Seattle, WA 98195-7240, United States
[b] Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, WA 98195-7720, United States
[c] Department of Genome Sciences, University of Washington, Seattle, WA 98195-7720, United States
[d] Division of Prevention and Population Sciences, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, United States
[e] Advanced Technologies and Surgery Branch, Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, United States
[f] Cerner Corporation, Kansas City, MO, United States
[g] Harvard-MIT Division of Health Sciences and Technology, Bioinformatics & Integrative Genomics, Cambridge, MA, United States
[h] Division of General Internal Medicine and McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University, Baltimore, MD, United States

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

Commentary

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

Brandon M. Welch [a,b,*], Karen Eilbeck [a,c], Guilherme Del Fiol [a], Laurence J. Meyer [d,e], Kensaku Kawamoto [a]

[a] Department of Biomedical Informatics, University of Utah, Salt Lake City, UT, United States
[b] Program in Personalized Health Care, University of Utah, Salt Lake City, UT, United States
[c] Department of Human Genetics, University of Utah, Salt Lake City, UT, United States
[d] Departments of Dermatology and Internal Medicine, University of Utah, Salt Lake City, UT, United States
[e] Department of Pediatrics, University of Utah, Salt Lake City, UT, United States

ARTICLE INFO

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
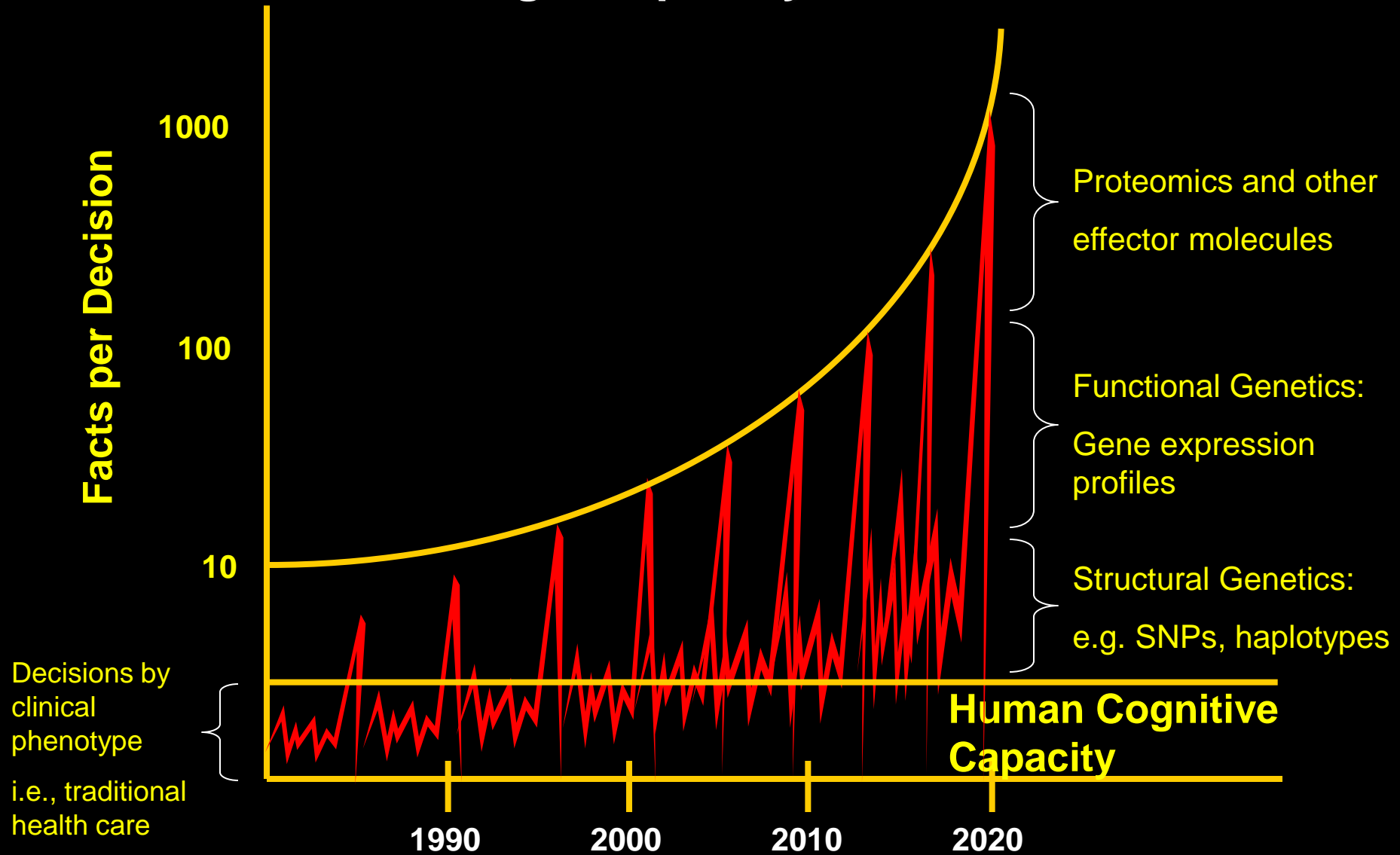
Keynote Talk Tip #3

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

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…
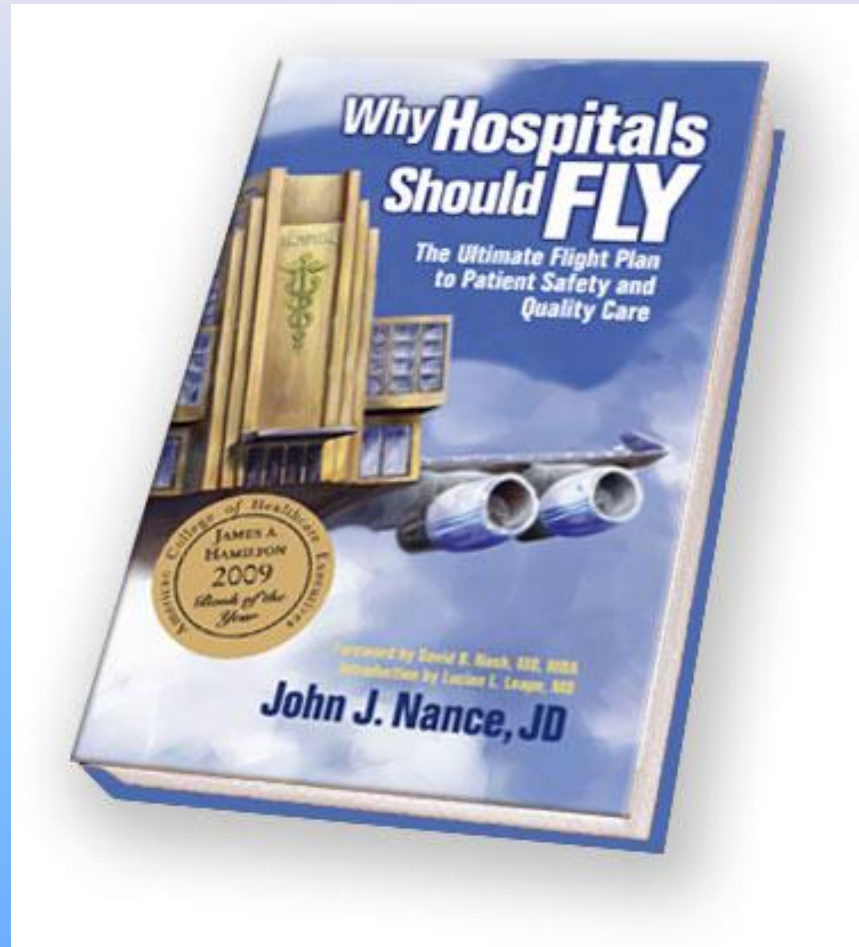
Industry-wide problem solving and rapid adoption of best practices

- The story of Three Mile Island

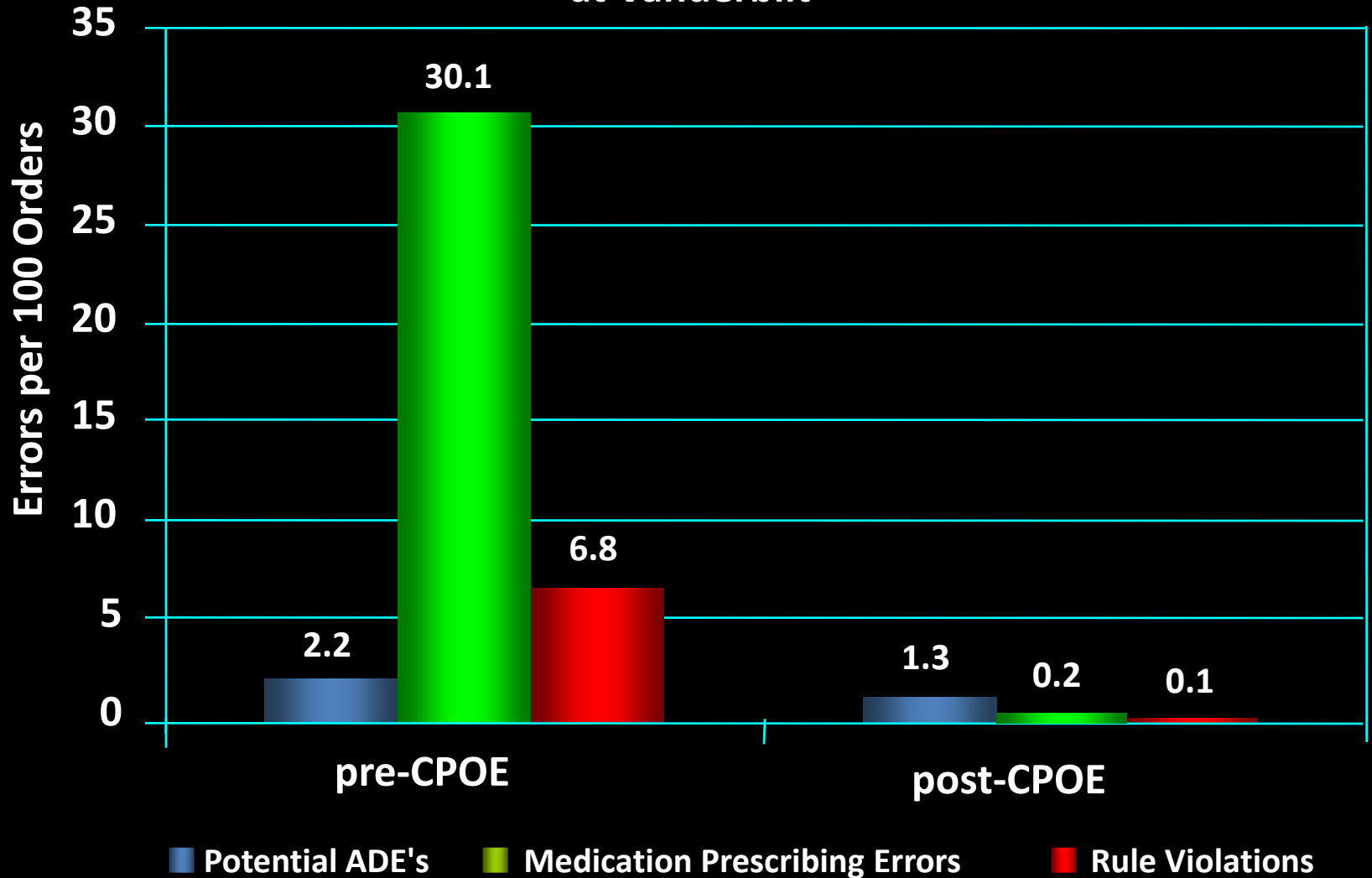"What happens to one of us happens to all of us"

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

Errors per 100 Orders

- pre-CPOE
  - 2.2
  - 30.1
  - 6.8
- post-CPOE
  - 1.3
  - 0.2
  - 0.1

■ Potential ADE's   ■ Medication Prescribing Errors   ■ Rule Violations

Potts, A. et al. PEDIATRICS 2004;:113:59-63
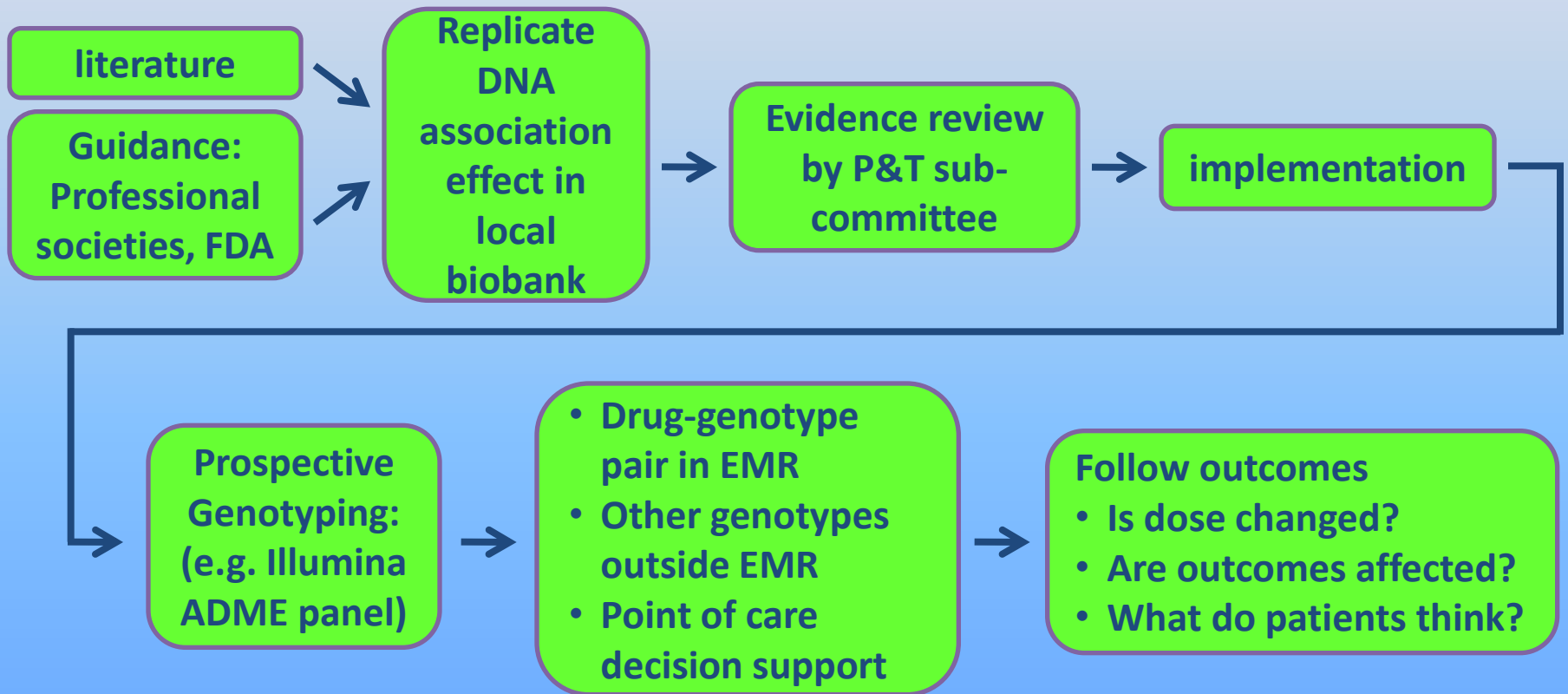
The scope of decision support

- "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

literature

Guidance: Professional societies, FDA

→ Replicate DNA association effect in local biobank

→ Evidence review by P&T sub-committee

→ implementation

→ Prospective Genotyping: (e.g. Illumina ADME panel)

→
- Drug-genotype pair in EMR
- Other genotypes outside EMR
- Point of care decision support

→ Follow outcomes
- Is dose changed?
- Are outcomes affected?
- What do patients think?

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:

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
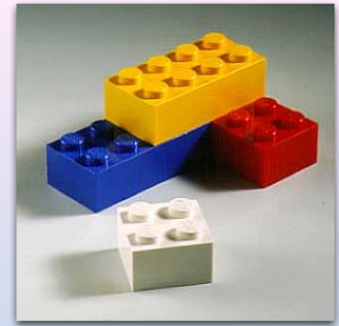
- Knowledge Representation Standards for interoperable electronic "decision support packages" containing:

    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
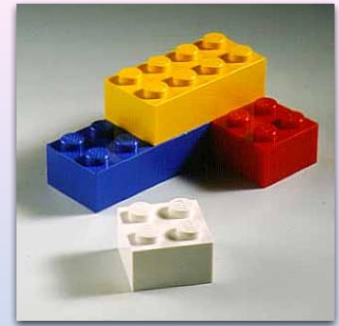
- Decision support authoring systems: tools to enable local clinicians to easily import, review, and implement decision support packages received from a Public Library of Decision Support packages

- 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.

Any fool can know.

The point is to understand.

Albert Einstein