

Real World Implementation of Precision Medicine

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IGNITE
www.ignite-genomics.org

G2MC
www.nas.edu/G2MC

APPLIED GENOMICS & PRECISION MEDICINE

IGNITE
Implementing GeNomics In pracTicE

Global Genomic Medicine Collaborative

Disclosure Information

Geoffrey S Ginsburg MD PhD

I have the following financial relationships to disclose

- Consultant/Advisor/Board Member for:
  Omicia, Pappas Ventures, Alere, Interleukin Genetics, CardioDx
- Grant/Research support from:

NHGRI, NHLBI, NCI, DARPA, USAMRIID, Gates Foundation, US Air Force, Henry Jackson Foundation, Singulex, IBIS Biosciences

- Stockholder in: CardioDx, Alere
- Employee of: Duke University

No Conflicts with the Current Presentation

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The Challenge

Using genomic information about an individual to optimize their clinical care

Human Genome Project

?

Precision Medicine & Health

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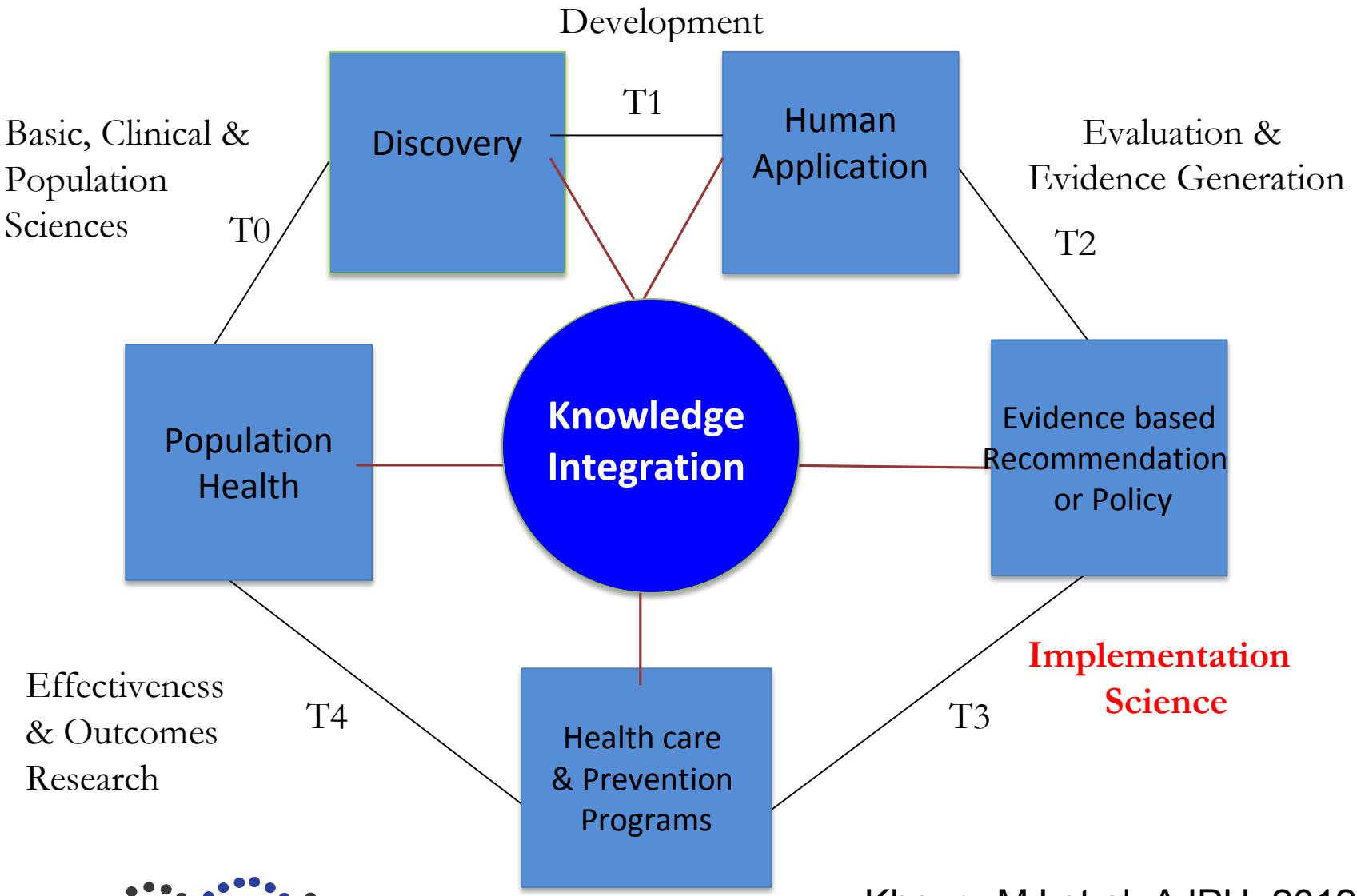
The (Non-Linear) Genomics Translation Research Cycle



Khoury MJ et al, AJPH, 2012

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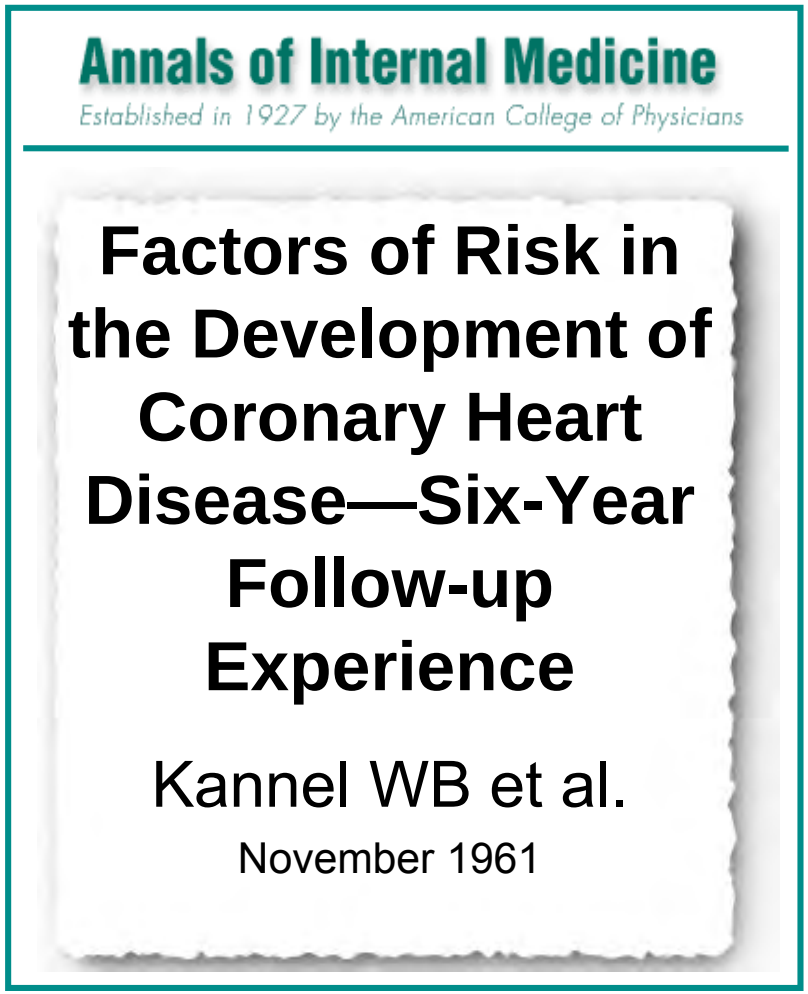
Early Precision Medicine: 1961 "Factors of Risk"



- High blood pressure
- Increased cholesterol
- Smoking
- Diabetes
- Family history
- Male sex

Source: Kannel WB et al. *Ann Intern Med* 1961;55:33−50.

(Failure of) Implementation of CVD Risk Calculators

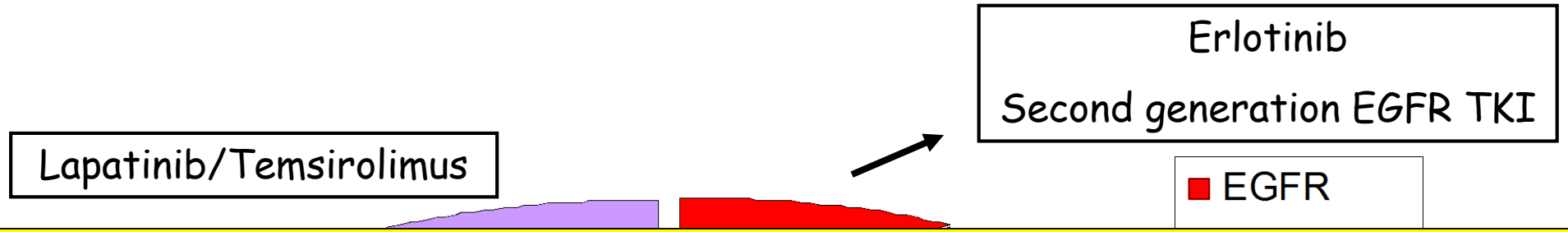
- Primary Care Physicians
  - only 13% had read guidelines carefully
  - only 17% used a CHD risk calculator

  "a large variability in knowledge, beliefs, and practice patterns among practicing family physicians"
- Barriers
  - Lack of knowledge
  - Distrust in validity
  - Time consuming

Eaton CB, *J Am Board Fam Med* 2006; 19:46–53.

Eichler K, *BMC Fam Pract* 2007; 8:1.

Lung Cancer: Molecular Guided Therapy



> 50% of non-small cell lung cancers have actionable mutations, but < 20% of non-small cell lung cancer patients are tested for EGFR in the USA (Lynch, Genet Med 2013)

Crizotinib vs. Chemotherapy

Crizotinib, 2nd Generation ALK Inhibitors

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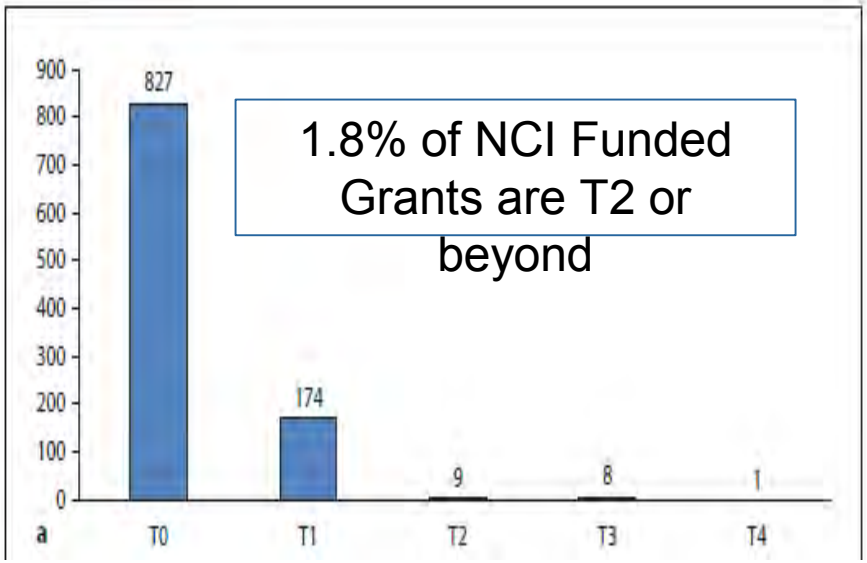
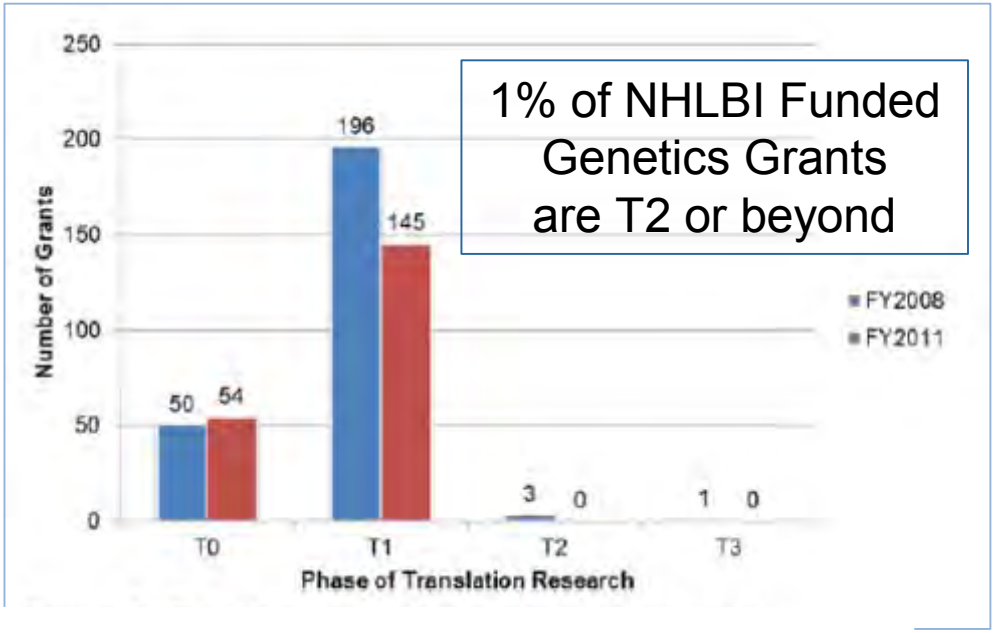
Genomics Translation: Funding Priorities for Evidence or Implementation ?



Schully, Public Health Genomics 2010

Puggal, Circ Cardiovasc Genet. 2013



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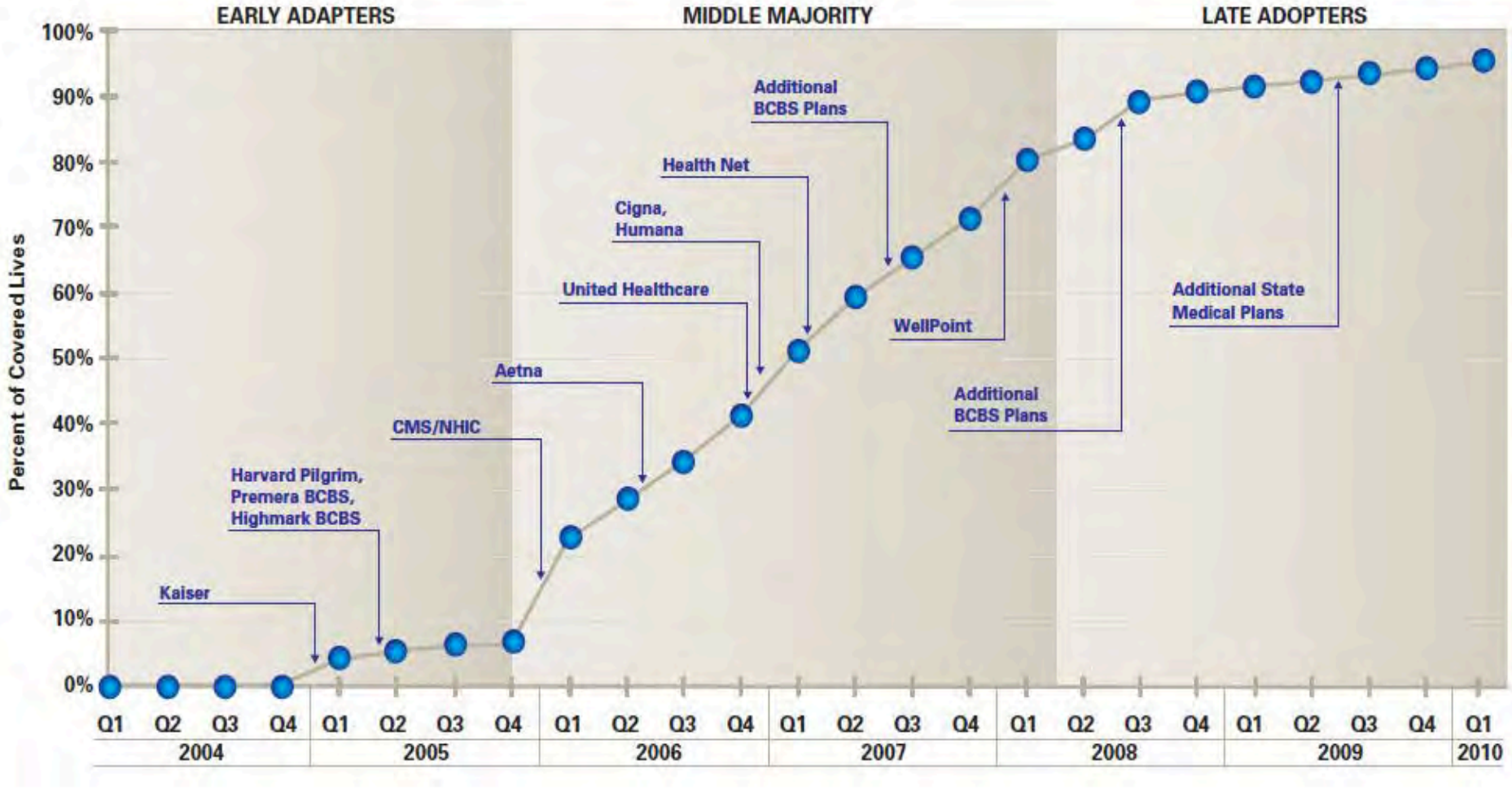
Payer Adoption of Oncotype DX®: Not All Payers are Alike



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COVERAGE INCONSISTENCIES FOR SAMPLE DIAGNOSTICS (2010)*

Innovative Test Examples	FDA Cleared?	Positive Coverage Policies			
		Aetna	Regional CMS	Cigna	Regional BCBS
AlloMap	Yes		✓		
Oncotype DX (breast Cancer)	No	✓	✓	✓	✓
MammaPrint	Yes		✓		
Pathwork Tissue of Origin	Yes				
BRACAnalysis	No	✓	✓	✓	✓
OVA1	Yes		✓		✓
KRAS (colorectal cancer)	No	✓	✓	✓	✓

*Note: All of these tests are offered as LDTs. The information in this table was current as of the publication of the source report in 2010, and has not been updated to reflect the most current information.

Source: BIO and Health Advances Report: The Reimbursement Landscape for Novel Diagnostics: Current Limitations, Real-World Impact, and Proposed Solutions. 2010.

First Genomic Medicine Meeting Report

- Much more happening than anticipated
- Largely in isolation
- Key barriers:
  - Lack of evidence
  - Interpretation of variants
  - Lack of expertise
  - Lack of standards
  - EMR integration
  - Financial model needed

Genet Med 2013; 15:258-67.

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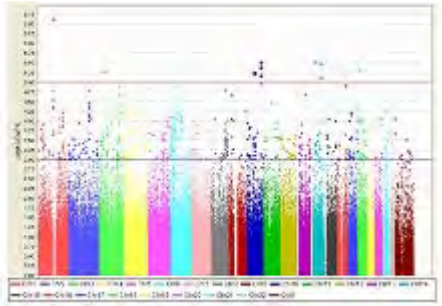
electronic MEdical Records and GEnomics (eMERGE) Network (https://emerge.mc.vanderbilt.edu/)



GWAS Discovery

Electronic Phenotyping

Consent Methodology

Clinician/Pt Education

Decision Support

Community Consultation

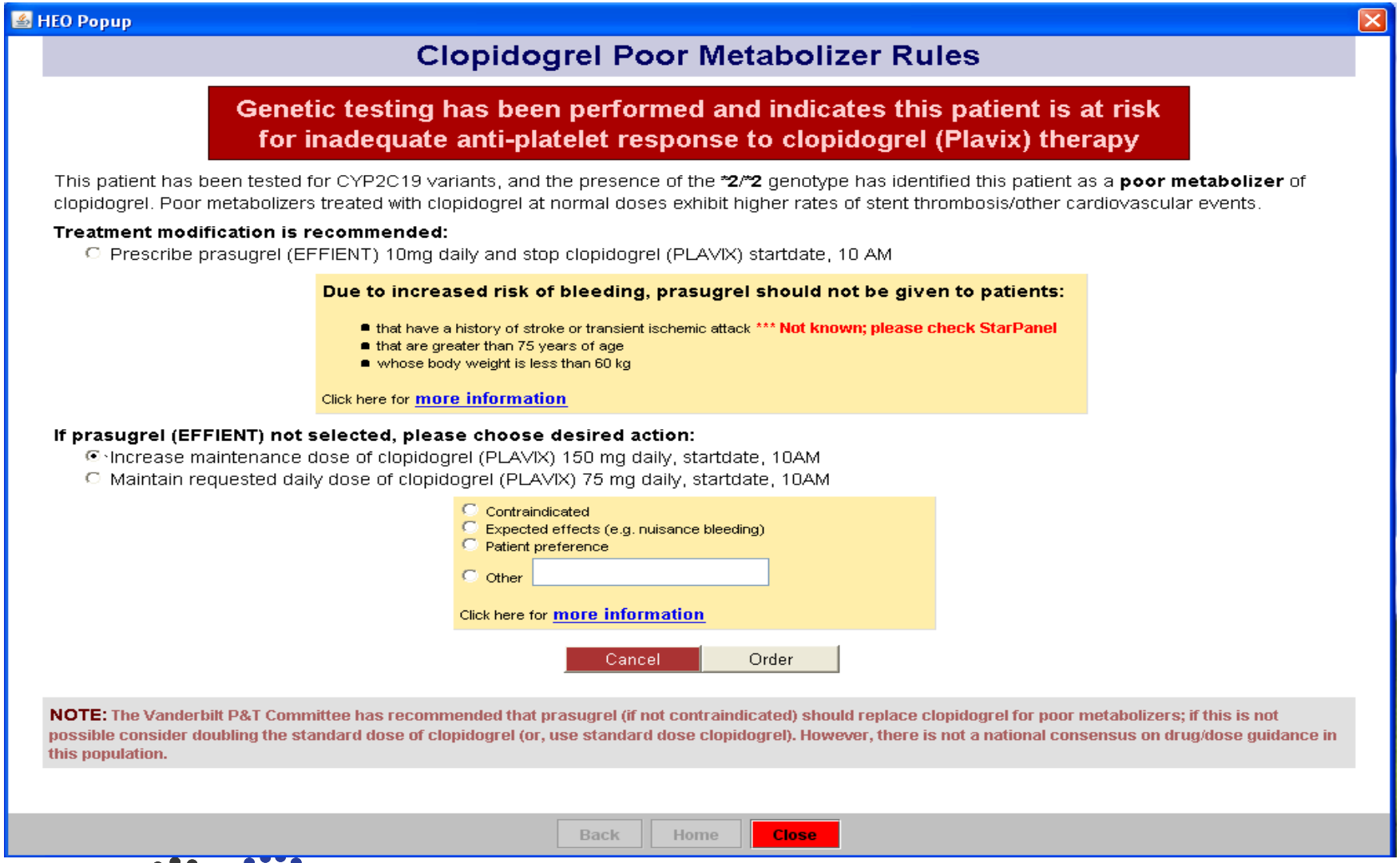
Pharmacogenomics

Pediatrics

Data Privacy

★ Phase I Sites ★ Coord. (ase II Sites ★ Pediatric Sites

Decision Support for Clopidogrel



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Courtesy Dan Roden, Vanderbilt

The National Academies of
SCIENCES · ENGINEERING · MEDICINE

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

ABOUT HMD | REPORTS | ACTIVITIES | MEETINGS

ACTION COLLABORATIVES

DIGITizE: Displaying and Integrating Genetic Information Through the EHR

To develop standards for integrating genomic patient data with other types of healthcare data in the EHR so that it becomes routine to deliver that information to providers and patients for patient care and to enable healthcare systems to generate evidence.

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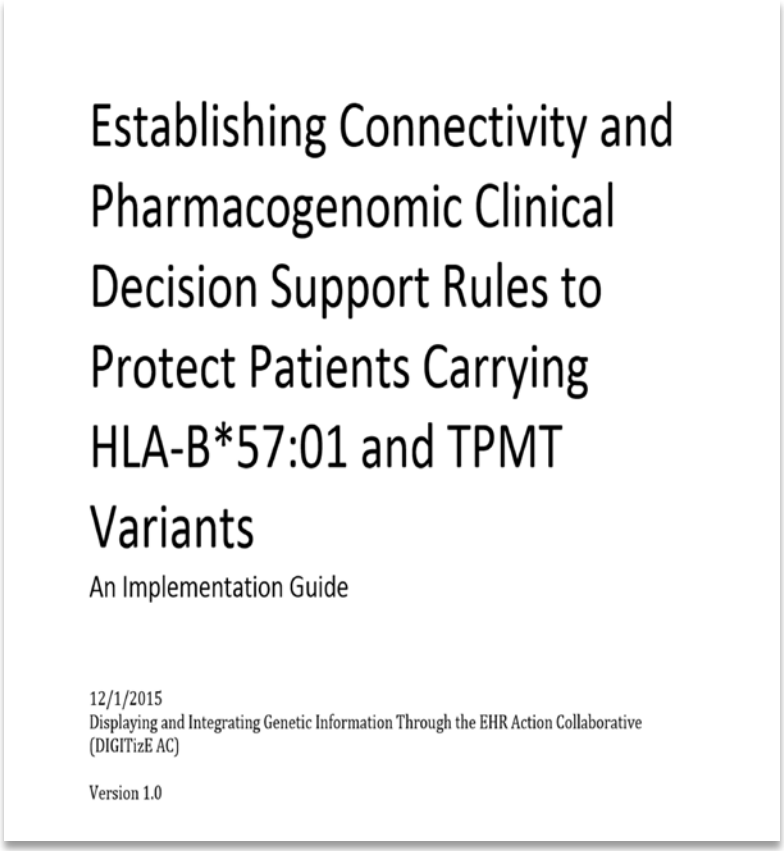
http://www.nationalacademies.org/hmd/Activities/Research/GenomicBasedResearch/Innovation-

DIGITizE: Standards for Genetic Information Integration into the EHR

- Government Agencies
- Providers
- Laboratories
- EMR Vendors
- Patients Representatives
- Standards Organizations


Establishing Connectivity and Pharmacogenomic Clinical Decision Support Rules to Protect Patients Carrying HLA-B*57:01 and TPMT Variants

An Implementation Guide

12/1/2015
Displaying and Integrating Genetic Information Through the EHR Action Collaborative (DIGITizE AC)

Version 1.0

- Rational
- LOINC Transfer Codes
- Suggested Rules

http://www.pgrn.org/pgx-news/annoucing-digitize-implementation-guide

Weitzel et al. BMC Medical Genomics (2016) 9:1
DOI 10.1186/s12920-015-0162-5

BMC Medical Genomics

RESEARCH ARTICLE Open Access

The IGNITE network: a model for genomic medicine implementation and research

Kristin Wiisanen Weitzel[1], Madeline Alexander[2], Barbara A. Bernhardt[3], Neil Calman[4], David J. Carey[5], Larisa H. Cavallari[1], Julie R. Field[6], Diane Hauser[4], Heather A. Junkins[7], Phillip A. Levin[8], Kenneth Levy[9], Ebony B. Madden[7], Teri A. Manolio[7], Jacqueline Odgis[7], Lori A. Orlando[10,19], Reed Pyeritz[3], R. Ryanne Wu[10,19], Alan R. Shuldiner[11,12], Erwin P. Bottinger[13], Joshua C. Denny[14,15], Paul R. Dexter[9], David A. Flockhart[9*], Carol R. Horowitz[16], Julie A. Johnson[1], Stephen E. Kimmel[2,17], Mia A. Levy[18], Toni I. Pollin[11], Geoffrey S. Ginsburg[19*] and on behalf of the IGNITE Network

- Expand and link existing genomic medicine efforts
- Develop implementation methods, in diverse settings and populations
- Contribute to evidence base regarding outcomes of incorporating genomic information into clinical care
- Disseminate best practices for genomic medicine implementation, diffusion, and sustainability

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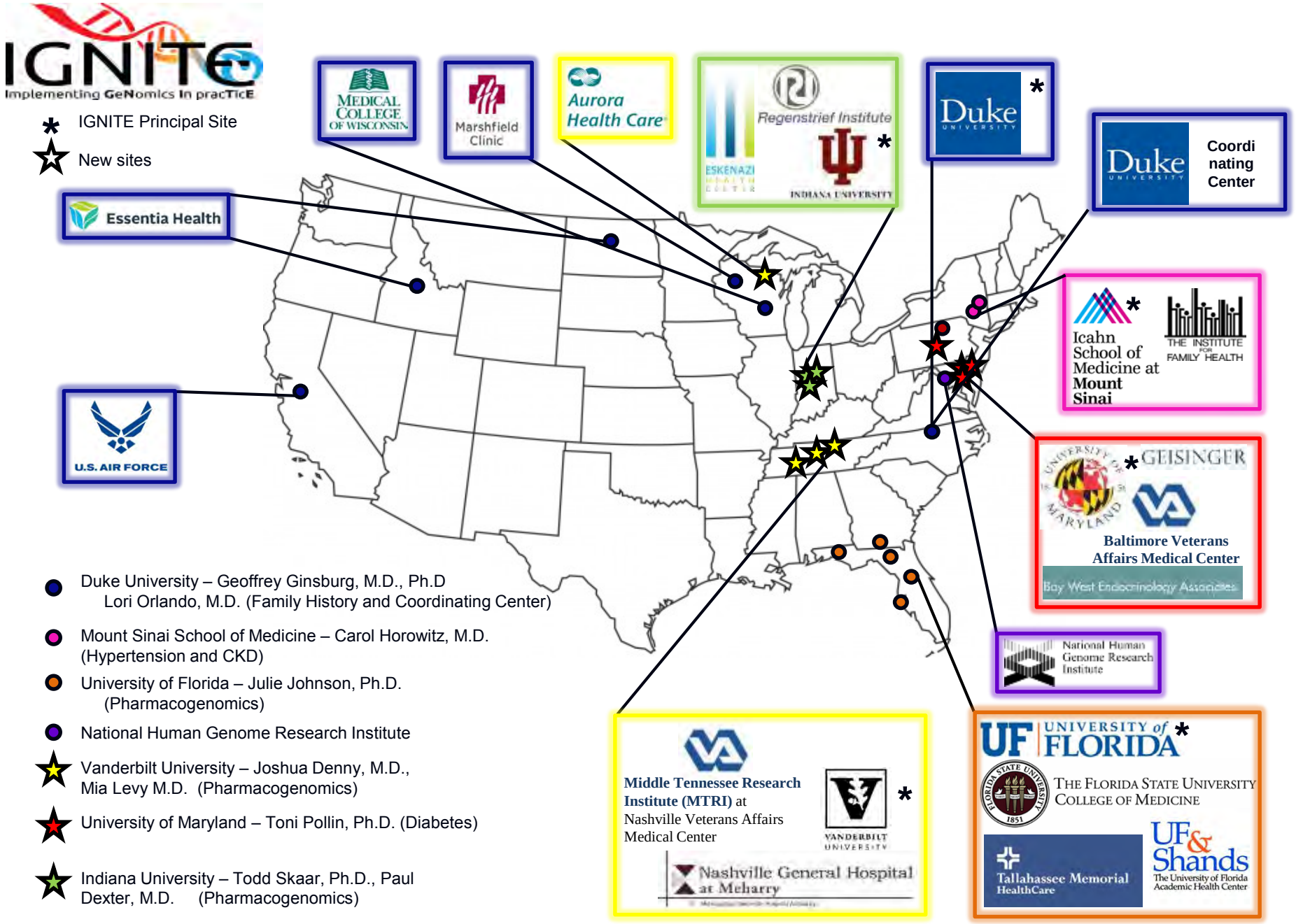
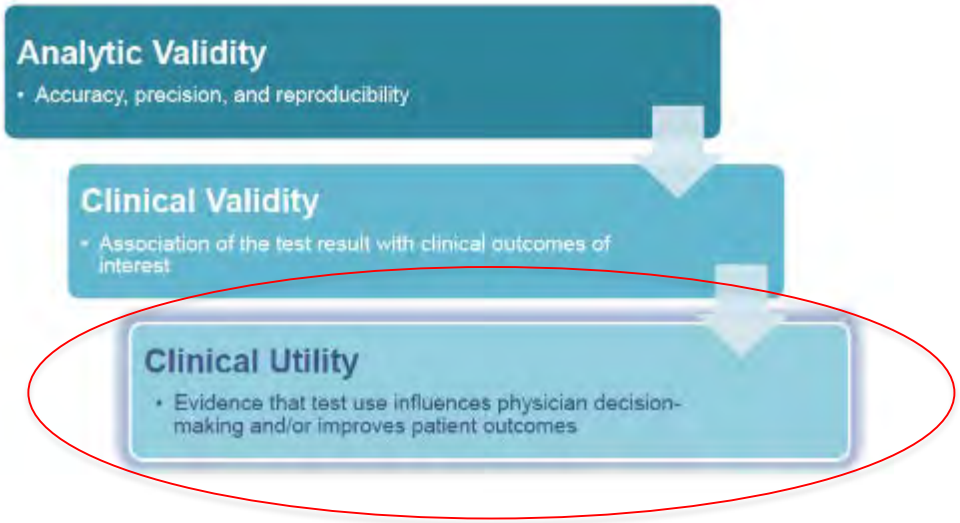


Courtesy Ebony Madden, NHGRI



6 Pilot Demonstration Projects Developing Implementation and Effectiveness Outcomes

Primary Care or Specialty Care Patient

Standard of Care → Outcome

Pragmatic Trials

Genomics-Guided → Outcome

Family History (80+ conditions)
Pharmacogenetics (Antiplatelet Agents, Pain, HCV)
Targeted Cancer Therapies
Genetic Risk (Apo L1, MODY)

Patient, Provider, System and Economic Outcomes

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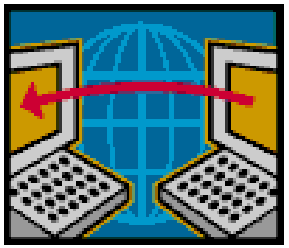
New Family Health History Platform (MeTree™)

Patient entry from home or clinic



Data sent to medical record, processed and report generated

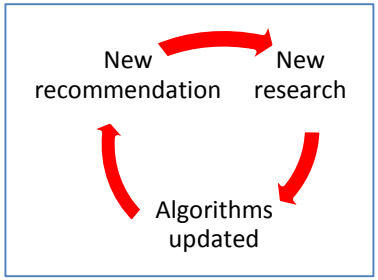
Appointment

Patient-Physician

Healthcare Plan

Prepare with worksheet to talk with relatives

Contact available for questions or problems



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SMART on FHIR®:

Medical apps that integrate into diverse EHR systems at the point of care

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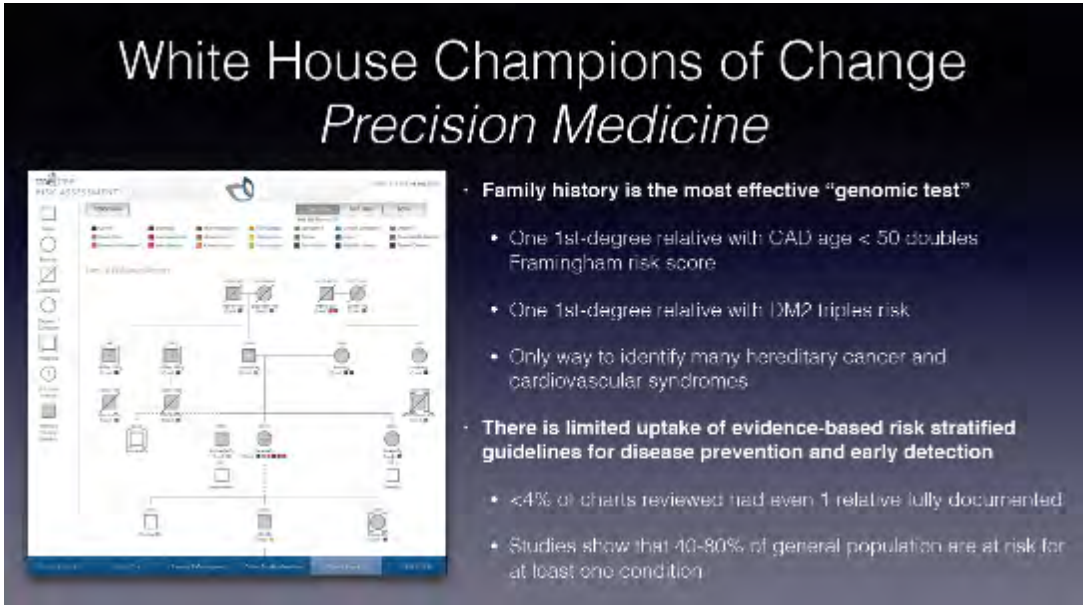

Implementation Stages

Pre-Implementation	Implementation	Post-Implementation
• **Identify current practice patterns**	• Assess implementation integrity (used as intended)	• Assess acceptance and satisfaction for stakeholders
• **Identify barriers & facilitators**	• Assess implementation exposure (used at intervention sites)	• Assess clinical impact for all stakeholders
• **Assess feasibility**	• Identify explanations and solutions for low integrity or intensity	• Adapt and finalize implementation strategy
• **Establish implementation plan**	• Modify implementation plan	• Assess impact of final implementation strategy

Adapted from Smith J, editor. Evaluation Methods in Implementation Research: An introduction. Implementation Science Meeting; 2010.

IGNITE: Implementation Outcomes and Measures

Outcomes	Measures
Model Reach	Representativeness of patient population to general population
Model Adoption	Representativeness of clinics agreeing to participate
Implementation Integrity	% time intervention used as intended
Implementation Exposure	% time intervention used
Maintenance and Sustainability	Cost to Implement Cost/Effectiveness

Mixture of Survey, EMR, and Qualitative da

IGNITE: Effectiveness Outcomes

	Patient	Provider	System
Emotional	• SF-12 (quality of life) • Patient Activation Measure • Prochaska Stage of Change • Satisfaction and anxiety • Quality of clinical encounter • Barriers to Model use	• Satisfaction • Knowledge • Barriers to Model use • Concur with CDS • Quality clinical encounter • Quality CDS for care	• Staff satisfaction • Organizational readiness to change (ORCA) • Implementation climate
Behavioral	• Medication adherence (Morisky) • % exercising (Stanford Brief Activity) • % eating 3 servings fruits/veggies per day (Rapid Food Screener) • % smoking • % ideal BMI • Implemented provider rec (uptake)	• Discussion of prevention • Discussion of risk • **% time CDS output used (uptake)** • **% adherence to CDS**	• Work flow/processes • Implementation policies and practices • Implementation climate • Intervention values and task fit
Biological	• **Demographics** • **FHH**	• **FHH documentation & counseling**	• **% completion MeTree™** • **time to complete FHH**
Clinical	• **Laboratory Data (i.e. LDL)** • **Screening tests performed** • **Screening complications** • **Vital Signs, Weight and BMI** • **Number of medications**	• **Disease control goals met** • **Referrals made**	• **% high risk patients** • **% w/ risk based screening** • **% w/ screening compl.** • **% w/ disease at goal** • **Visit length/Wait times**
Financial	• **Socio-economic status** • **Medication costs**		• **Office/ ER visits, hospitalizations** • **Model resource needs** • **Impact on family members**

Mixture of EMR (blue) and survey data

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IGNITE:
Common Challenges and Solutions

1) **Clinician knowledge**

- all projects developed educational materials and conducted educational meetings for clinicians

2) **Integration with the electronic health record**

- health system level adoption of genomic standards
- development of clinical decision support and access

3) **Engaging diverse patient and clinician populations**

- Forming genomics medicine advisory board to represent stakeholders and involve them in every step

3) **Recruiting patients**

- actively involve patients in implementation (e.g., a patient advisory board to develop educational materials) and develope materials to inform patients about questions to ask their clinician or payer

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Sperber et al – in preparation

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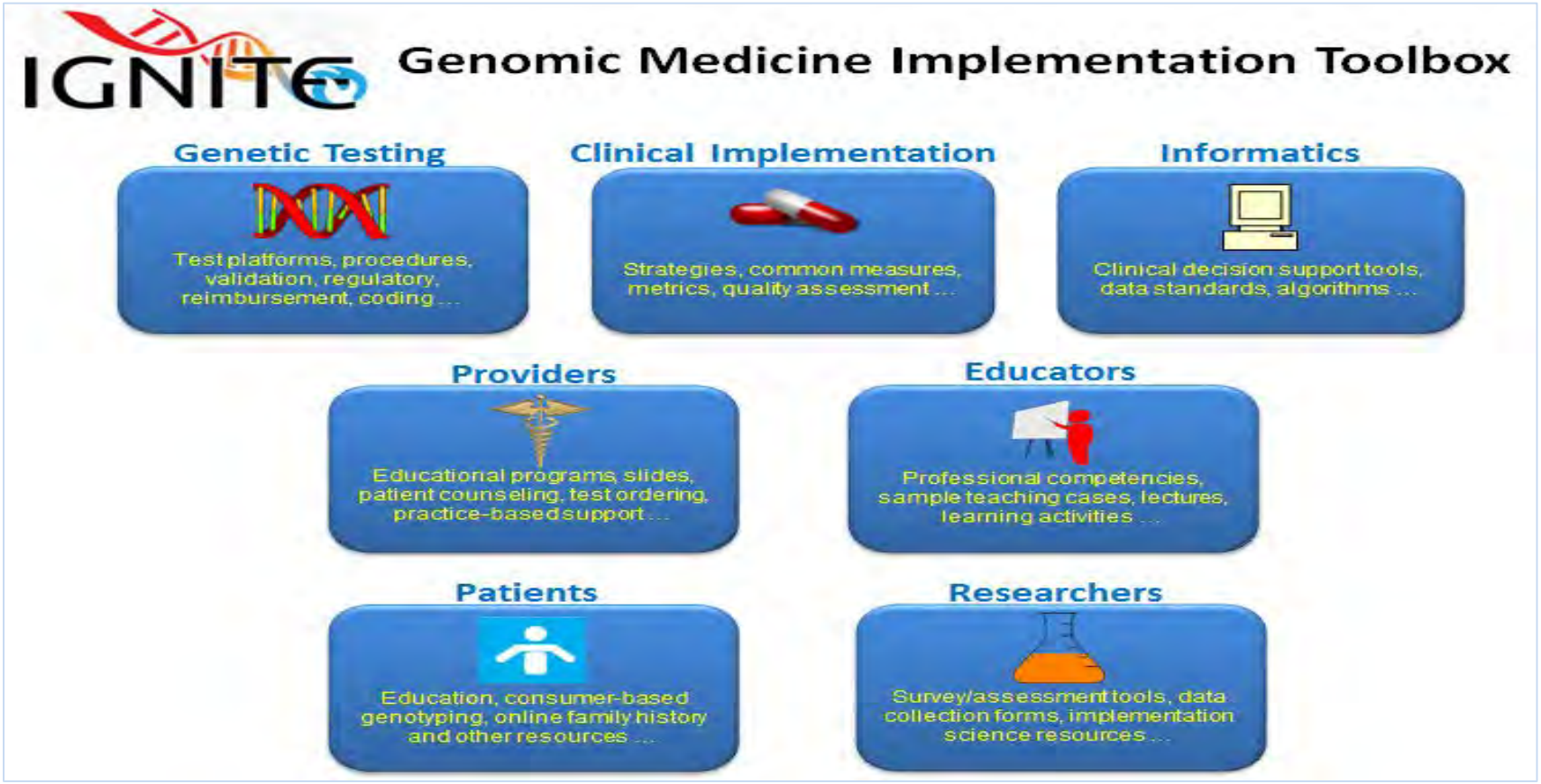
The IGNITE Toolbox

To disseminate best practices in the implementation of genomic medicine



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Global Genomic Medicine Collaborative (G2MC)

PERSPECTIVE

POLICY

Global implementation of genomic medicine: We are not alone

Teri A. Manolio,[1*] Marc Abramowicz,[2] Fahd Al-Mulla,[3] Warwick Anderson,[4] Rudi Balling,[5] Adam C. Berger,[6] Steven Bleyl,[7] Aravinda Chakravarti,[8] Wasun Chantratita,[9] Rex L. Chisholm,[10] Vajira H. W. Dissanayake,[11] Michael Dunn,[12] Victor J. Dzau,[13] Bok-Ghee Han,[14] Tim Hubbard,[15] Anne Kolbe,[16] Bruce Korf,[17] Michiaki Kubo,[18] Paul Lasko,[19] Erkki Leego,[20] Surakameth Mahasirimongkol,[21] Partha P. Majumdar,[22] Gert Matthijs,[23] Howard L. McLeod,[24] Andres Metspalu,[20] Pierre Meulien,[25] Satoru Miyano,[26] Yaakov Naparstek,[27] P. Pearl O'Rourke,[28] George P. Patrinos,[29] Heidi L. Rehm,[30] Mary V. Relling,[31] Gad Rennert,[32] Laura Lyman Rodriguez,[1] Dan M. Roden,[33] Alan R. Shuldiner,[34] Sukdeb Sinha,[35] Patrick Tan,[36] Mats Ulfendahl,[37] Robyn Ward,[38] Marc S. Williams,[39] John E. L. Wong,[40] Eric D. Green,[1] Geoffrey S. Ginsburg,[41*]

Sci Trans Med 2015

- > 35 nations
- Explore synergies, redundancies, collaborative opportunities for implementation of genomics into medicine
- Opportunities to advance the genome sciences as an agenda to impact global health

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Global Genomic Medicine Collaborative

G2MC 2015: Large Scale Genomics Initiatives

- Genomics England
  - 100,000 genomes (Linked to NHS EMR data)
- Geisinger - Regeneron (USA)
  - 100,000 genomes (Linked to EPIC EMR data)
- Genome Qatar
  - 300,000 Qatari genomes (Linked to CERNER EMR data)
- Estonian Genome Project
  - 52,000 genomes (Linked to health care data)
- The US Precision Medicine Initiative
  - ? 1,000,000 Genomes (Linked to EMR and mHealth data)
- Initiating efforts in Korea, Malaysia, Scotland, Singapore

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A Grand Challenge…
for Implementation of Genomic Medicine

Using genomic information about individuals to optimize clinical care *and population health*

Genomics england

?

Millions of Genomes

Evidence Generation/Economic Models
Data Sharing/Security
Implementation Incentives
Workforce Development
Participant Engagement/Trust

Precision Medicine & Population Health

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Questions?

Please submit your question in the Q&A feature on the right of the interface. Type and press submit.

U.S. Department of Health and Human Services

National Institutes of Health | National Cancer Institute

http://cancercontrol.cancer.gov/research-emphasis/precision-medicine.html

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