Genomics and Patient Safety: Practical Applications for Pharmacogenomics

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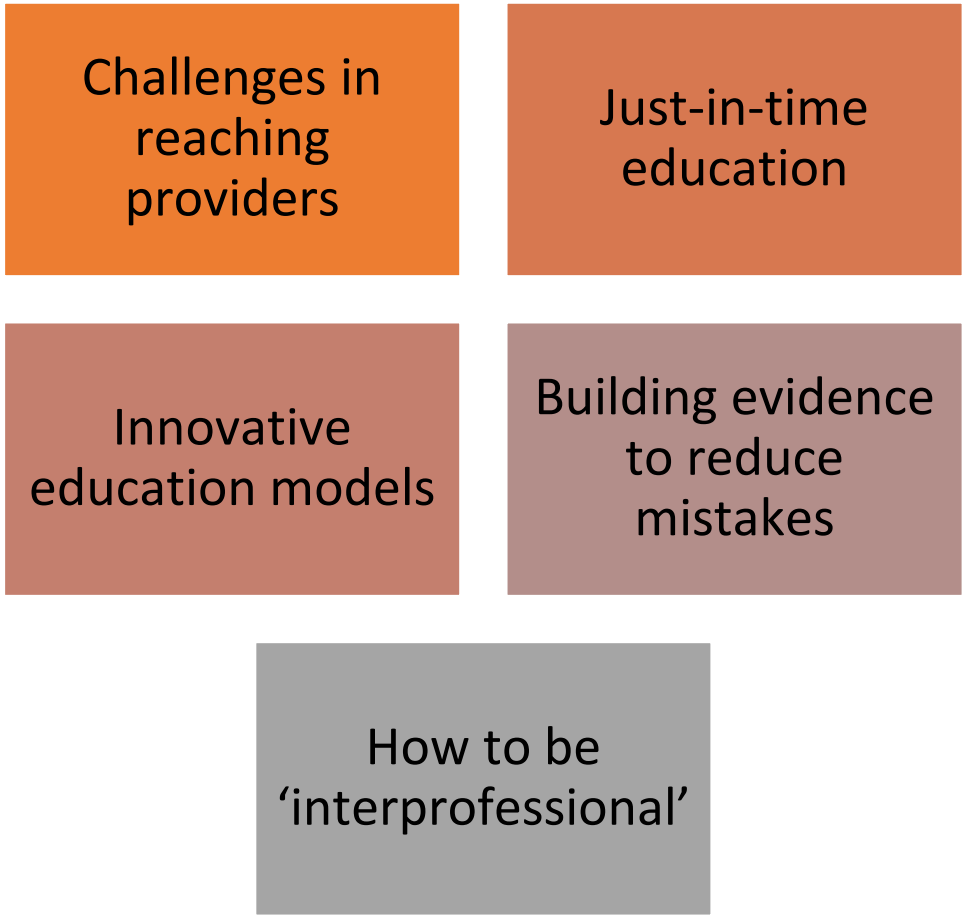
"All I'm saying is ***now*** is the time to develop the technology to deflect an asteroid."

Overview

- Evaluate opportunities to evolve CME delivery amidst genomic advances and ongoing health care transformation
- Describe regional and national KP efforts to implement genomic medicine that optimizes patient safety and provider satisfaction
- Produce actionable takeaways based on these experiences thus far…

IOM Genomics Roundtable

- Recent workshop in August, 2014
- “Improving Genetics Education in Graduate and Continuing Health Professional Education: Workshop Summary"



Takeaways: How to Evolve

- David Davis, Senior Director, Continuing Education and Performance Improvement, AAMC

- *More effective means – such as just-in-time learning – are available and increasingly relevant*
- *CME should be more interprofessional*
- *Should leverage existing initiatives (i.e., PROCEED, MedEdPortal)*

Takeaways: Just-in-time Approach

- Benjamin Raby, Section Editor – Genetics, UpToDate
- Associate Professor of Medicine
- Channing Division of Network Medicine and the Division of Pulmonary and Critical Care Medicine,
- Director, Brigham and Women's Hospital Pulmonary Genetics Center Harvard Medical School

- *Critical need to incorporate disease-specific genetic information rapidly*
- *UpToDate makes educational information accessible through electronic medical records*
- *Biggest challenge is the 'lag' between reports of translational findings and integration into practice*

Takeaways: IPE

- Diane C. Seibert, Professor, Chair & Director, Family Nurse Practitioner Program
- Uniformed Services University

- *The concept of IPE is to learn about what another profession does, with other professionals in the same environment, and taught from different professions*
- *IPE is useful because health care systems are so complex that different perspectives are needed to get the best outcomes*

Medical Practice Realities

Most physicians deliver only 55% of recommended care

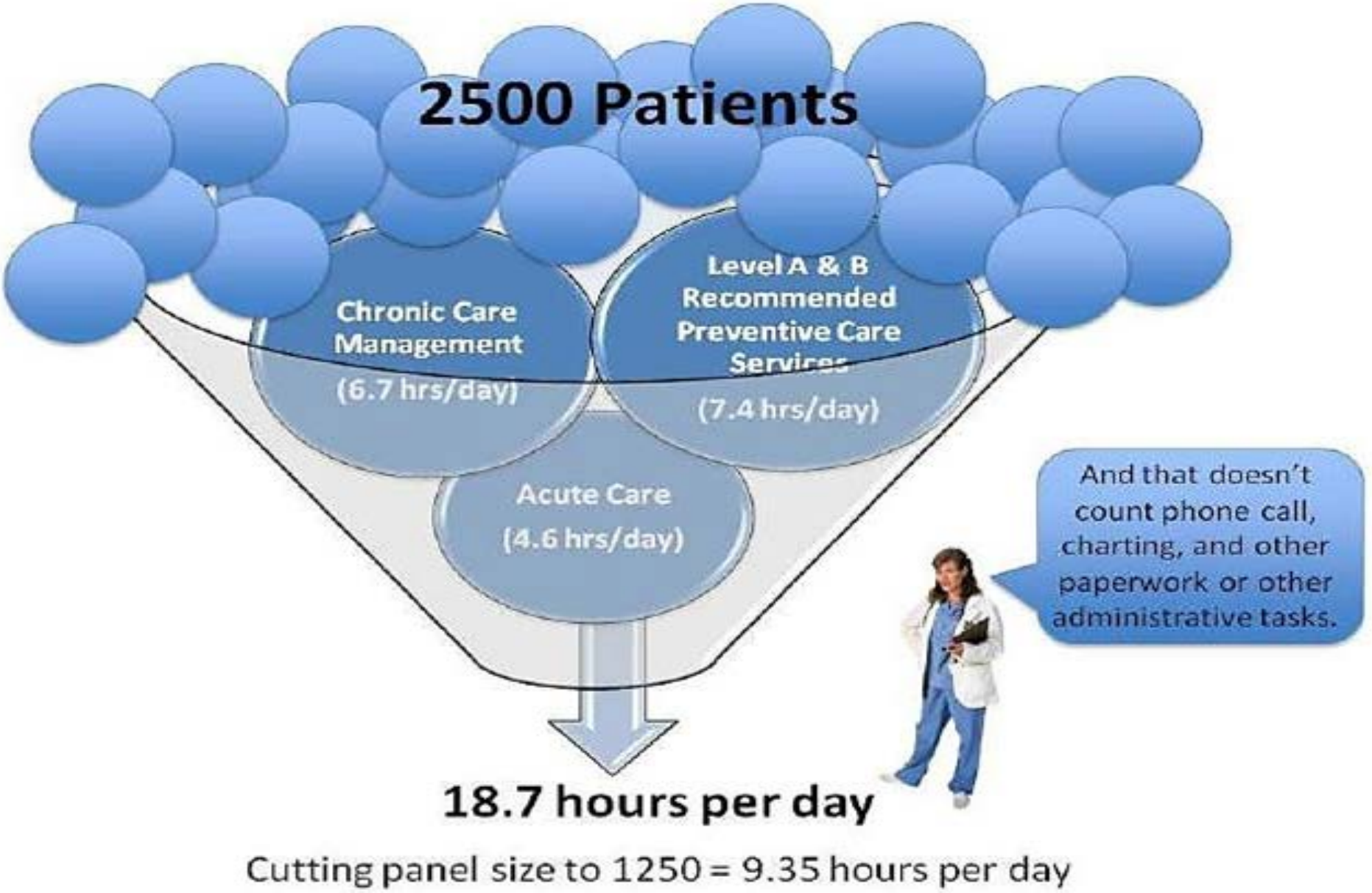
- 42% report not enough time with their patients

Pharmacist protocols for approval of medication refills free up physician time

Providers spend 13% of their day on care coordination

- Only half of their time on activities using their medical knowledge.
- MTM telepharmacy services during transitions of care improve physician efficiency

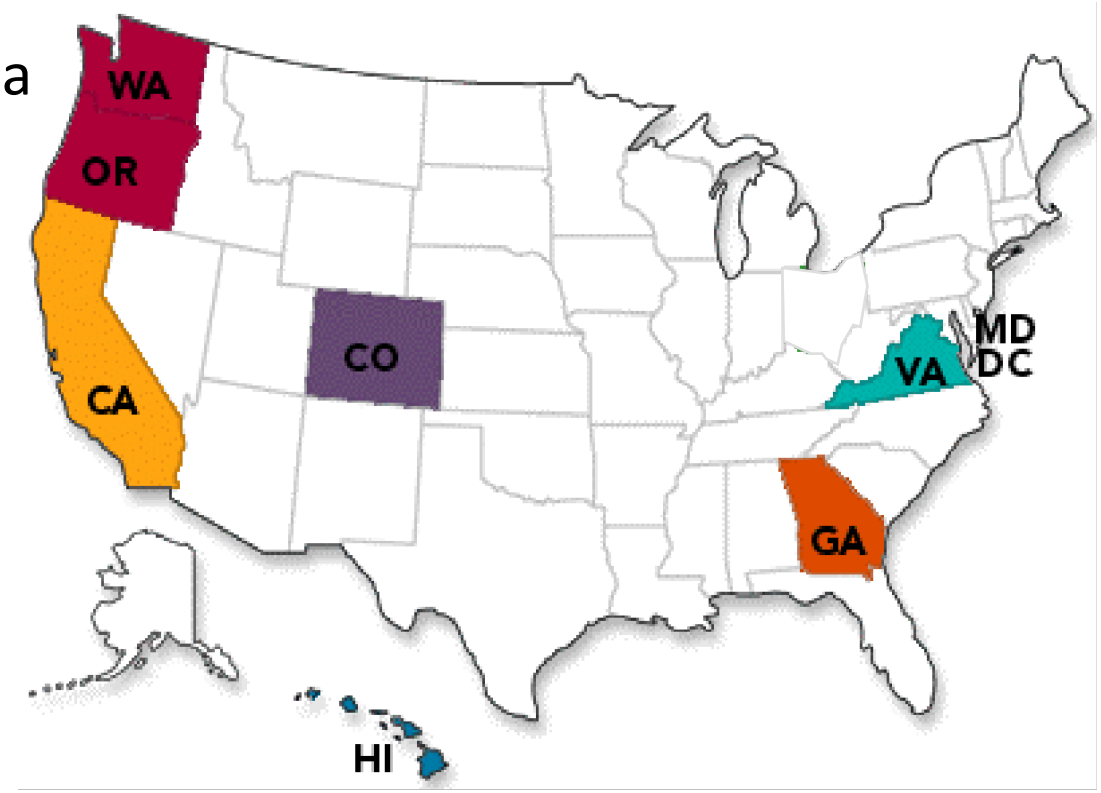
Time demands on primary care physicians…



Østbye T, Yarnall KS, Krause KM et al. Is there time for management of patients with chronic diseases in primary care? *Ann Fam Med.* 2005;3:209-14

KP National Program – By the numbers…

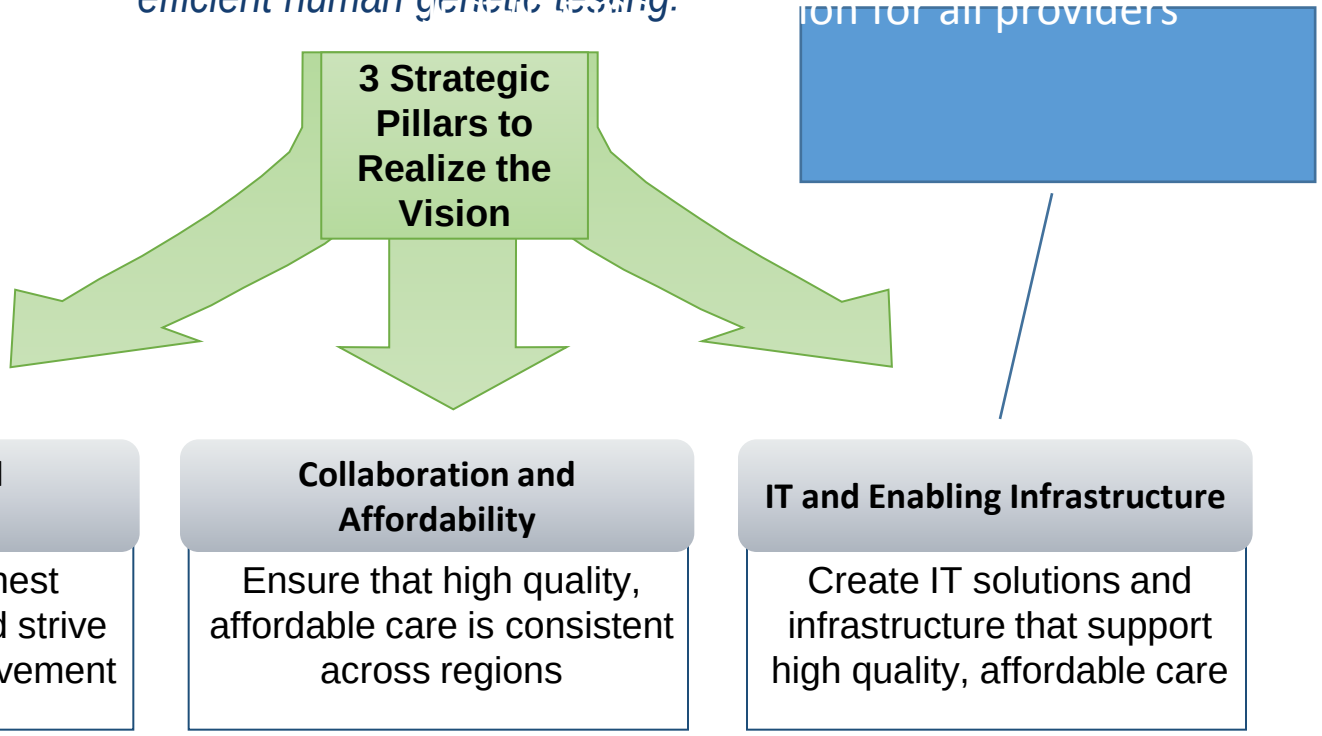
- 7 regions serving 8 states and the District of Columbia
- Over 9 million members
- 174,000 employees
- Over 16,000 physicians
- Over 48,000 nurses
- 38 hospitals
- 611 medical offices and other facilities
- $50 billion operating revenue (2012)



A little history on the KP's Genetic Strategy

Genetics Services Vision Statement

Kaiser Permanente provides clinical genetic and testing services to guide personalized evidence-based care decisions and care delivery. Our team-based approach enlists clinical expertise, information technology and cross regional collaboration to support high quality, reliable and efficient human genetic testing.



Why are we here?

We need a team based approach to genetic testing and selection in Oncology

Themes			
Oncologists	Geneticists	Laboratory	Pharmacy
Multiple areas of specialization Hundreds of clini trials Laboratory par tests changing ra – Need pathology molecular testing experts to help us select the right tests and panels	Som	most accurate results, fastest TAT and most affordable price	The FDA continues to pair genetic tests with ncer treatments mpanies ng free tests may be a flict of interest. Need lab to evaluate quality

David Baer, MD – "We (oncologists, lab directors, geneticists, pathologists, pharmacists) have to all stop saying it's not our job and start working collaboratively to figure this stuff out."

Interregional Genetic Testing Resource Plan

Focus on expanding the value to Oncologists

- Pharmacogenomics
- Oncology
- Regular updates

- Intuitive to use
- Establish access
- Incorporate its use

- Improve decision making
- Speed the application of new evidence for patients
- Improve the consistency of care

Interregional Genetic Testing Resource

Oncologists may want to see only cancer related tests and all test lists have the capability to search for a specific test of interest

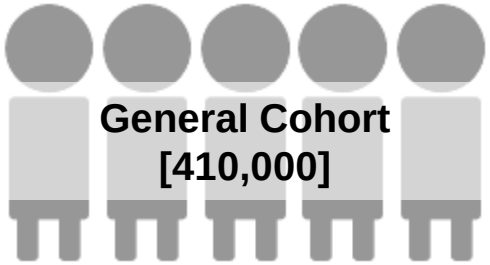
This view shows genetic tests that are relevant to **Oncology**:

⊕ new item or edit this list

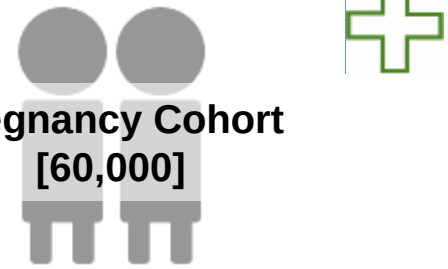
All Items By Test Type Oncology ... Colorectal ×

✓	Test Name		Gene/Locus	Test Description	Condition Name	KP Internal Regions	Genetic Test Type
	BRAF (V600E) mutation analysis (Qualitative)	...	*BRAF*	Detects the most common activating *BRAF* mutation in melanoma tissue.	Melanoma	NCAL	Molecular - Somatic
	EGFR Tumor Screening	...	*EGFR*	Identifies somatic EGFR mutations in tumor tissue.	Metastatic colorectal cancer (mCRC)	NCAL	Molecular - Somatic
	Epidermal Growth Factor Receptor (EGFR) Pathway Mutation Analysis (KRAS, BRAF)	...	*BRAF*, *KRAS*	Detects mutations in codons 12,13, and 61 of *KRAS* and the *BRAF* V600E mutation as part of the EGFR pathway.	Metastatic Colorectal Cancer; Squamous Cell Carcinoma of the Head & Neck	NCAL	Molecular - Somatic
✓	Hereditary Colorectal Cancer Syndrome Panel	...	*EPCAM*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, +	Next generation sequencing panel that at least includes the 5 genes known to cause Lynch Syndrome, plus genes associated with other hereditary colorectal cancer syndromes.	Lynch syndrome and other hereditary colon cancer syndromes		Molecular - Germline

The KP Research Bank will have samples from 500k members

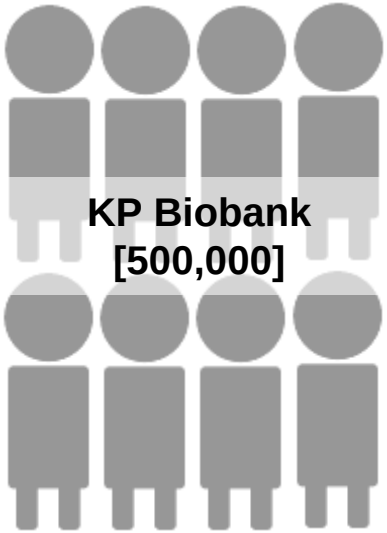


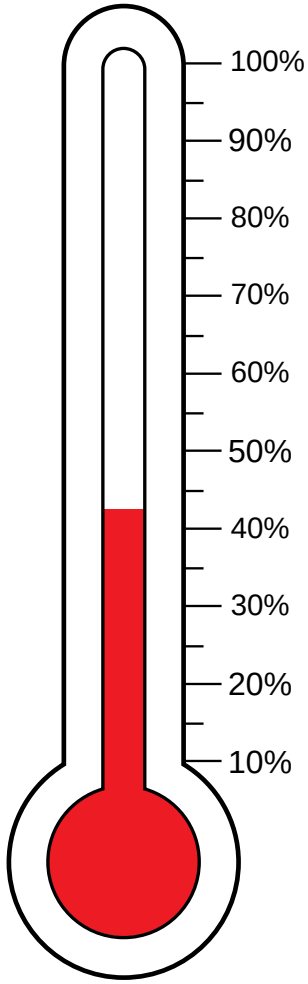
Enables research of relevance to all KP members across a broad spectrum of common diseases and builds on existing 200,000 samples



Will be among the largest and richest pregnancy research cohorts in the world

Linked to tissue banks; Oncology is an early adopter of genomic medicine; over half of KP researchers focus on cancer

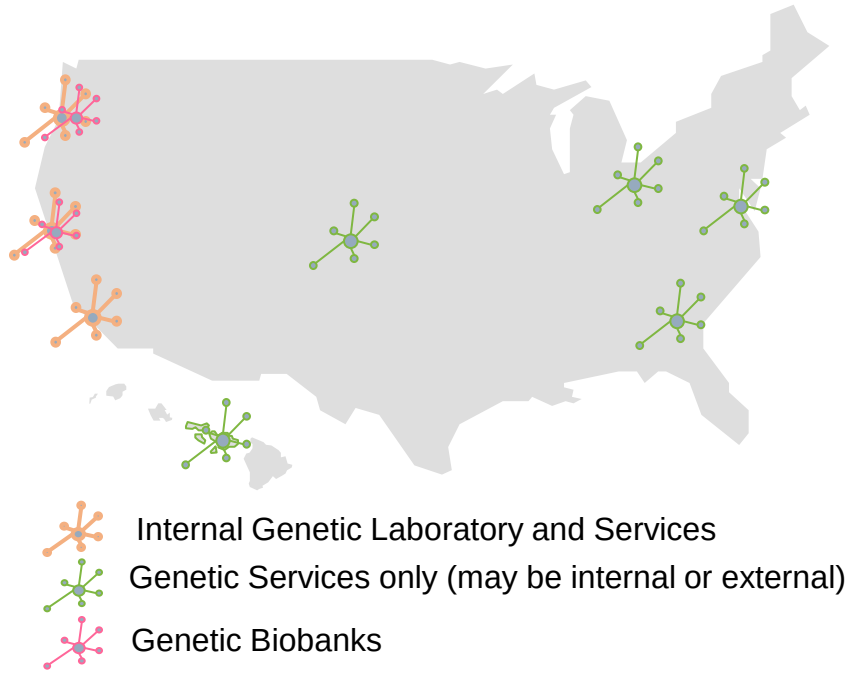




KP National Program – Building Connections

Goals for 2015

- Draft a "roadmap" of resources and champions in each KP region for pharmacogenomics
- Provide content expertise to help guide implementation and research

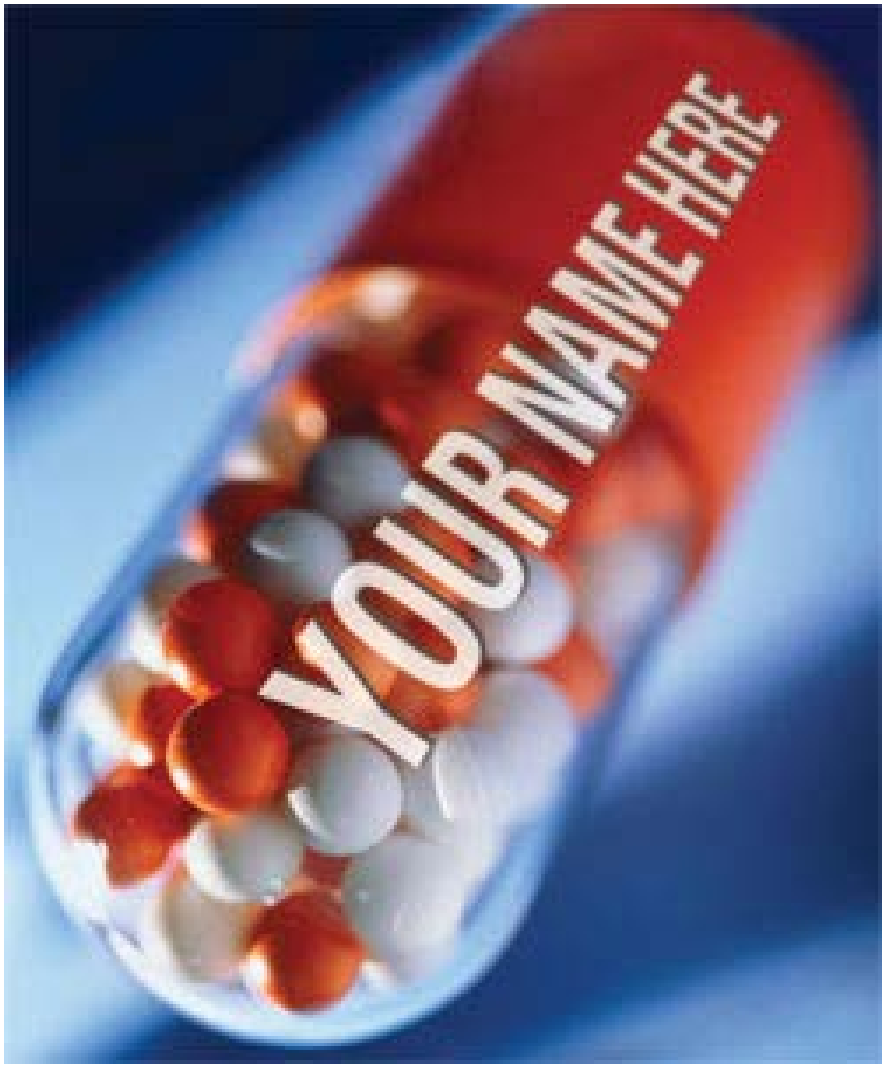


Kaiser Permanente Colorado

- Colorado's largest nonprofit health plan
- 28 Medical Offices
  - 6,000+ staff and physicians
  - 635,000 members
- Recognized by the National Committee for Quality Assurance (NCQA) as the top-ranked private health plan in Colorado and No. 13 in the entire nation for 2013-2014
- 22 KPCO clinics and more than 300 individual physicians have earned the top-level Patient-Centered Medical Home designation from the National Committee for Quality Assurance (NCQA)

Precision Medicine

- Includes applied Pharmacogenomics (PGx)
- Part of a systematic approach to optimizing pharmacotherapy
- Recent comments by President Obama during SOTU address augment current translational efforts

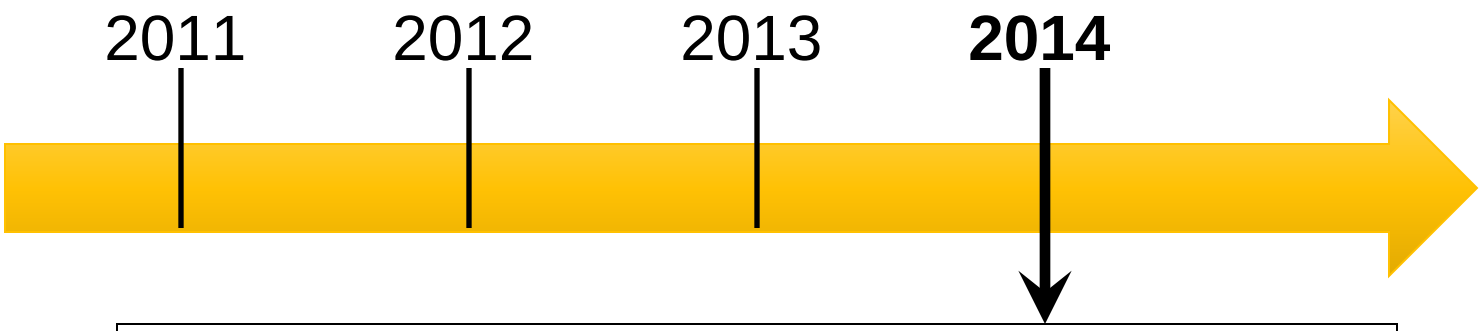


KPCO Regional Goals

Promulgate use of evidence-based technology to optimize patient safety:

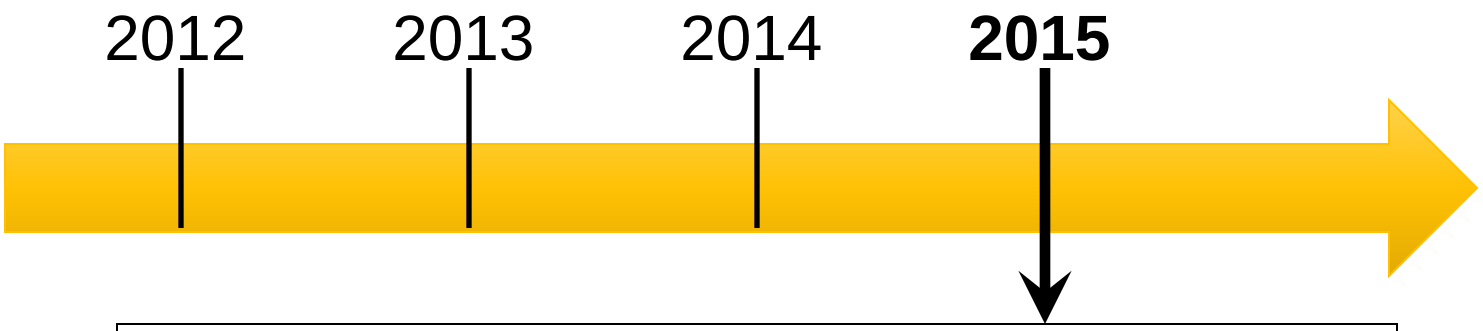
1. Prevent avoidable adverse drug reactions
2. Promote and increase medication adherence
3. Provide targeted educational information to front-line clinical providers about impact of pharmacogneomics

KPCO Implementation Roadmap



- Became National KP Co-Lead for PGx
- Implemented targeted *CYP2C19* genotyping for clopidogrel
- Developed proposal for embedded just-in-time education for front-line clinicians re: *CYP2C19*-clopidogrel interaction

KPCO Implementation Roadmap



- Expanding Clinical Testing with PGx Panel (6 genes, pre-emptive screening) to identify impact on healthcare related utilization and provider satisfaction
- Developing proposal for front-line provider education to increase engagement and collaboration

Interim Data Summary for KPCO

- 219 patients approached for *CYP2C19* genotyping (post-ACS, stent implantation)
- 149 patients completed testing
- ***77 (~52%) of patients had an actionable genotype*** (e.g. carried at least one gain-of-function or loss-of-function allele)
- Clinical Pharmacy recommendations accepted 100% of the time.

Interim Data Summary for KPCO

- 37 patients diagnosed with inherited Long QT Syndrome (LQTS)
- *13 (~35%) of patients had an active Rx* for a drug with known QT-prolongation effects
- Comprehensive medication reviews for all patients, with consult/recommendations forwarded to all downstream providers
- Problem list updated for all patients

Examples of Outside Resources

Clinical Pharmacogenetics Implementation Consortium Guidelines for *CYP2C9* and *VKORC1* Genotypes and Warfarin Dosing

JA Johnson[1], L Gong[2], M Whirl-Carrillo[2], BF Gage[3], SA Scott[4], CM Stein[5], JL Anderson[6], SE Kimmel[7,8,9], MTM Lee[10], M Pirmohamed[11], M Wadelius[12], TE Klein[2] and RB Altman[2,13]

Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Codeine Therapy in the Context of *Cytochrome P450 2D6* (*CYP2D6*) Genotype

KR Crews[1], A Gaedigk[2], HM Dunnenberger[3], TE Klein[4], DD Shen[5,6], JT Callaghan[7,8], ED Kharasch[9] and TC Skaar[7]

Clinical Pharmacogenetics Implementation Consortium Guidelines for Cytochrome P450-2C19 (*CYP2C19*) Genotype and Clopidogrel Therapy

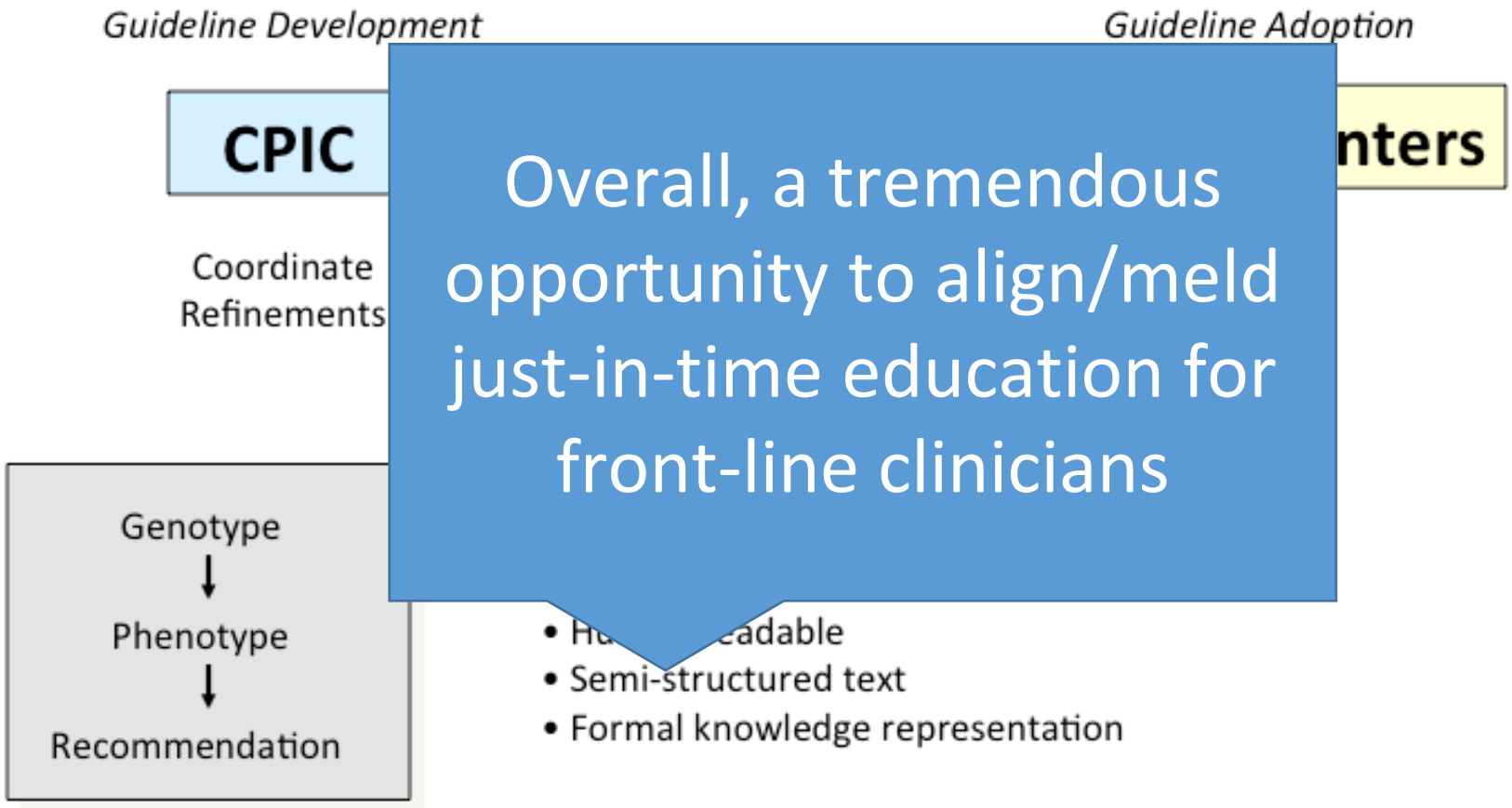
SA Scott[1], K Sangkuhl[2], EE Gardner[3], CM Stein[4,5], J-S Hulot[6,7], JA Johnson[8,9,10], DM Roden[11,12], TE Klein[2] and AR Shuldiner[13,14]

The Clinical Pharmacogenomics Implementation Consortium: CPIC Guideline for *SLCO1B1* and Simvastatin-Induced Myopathy

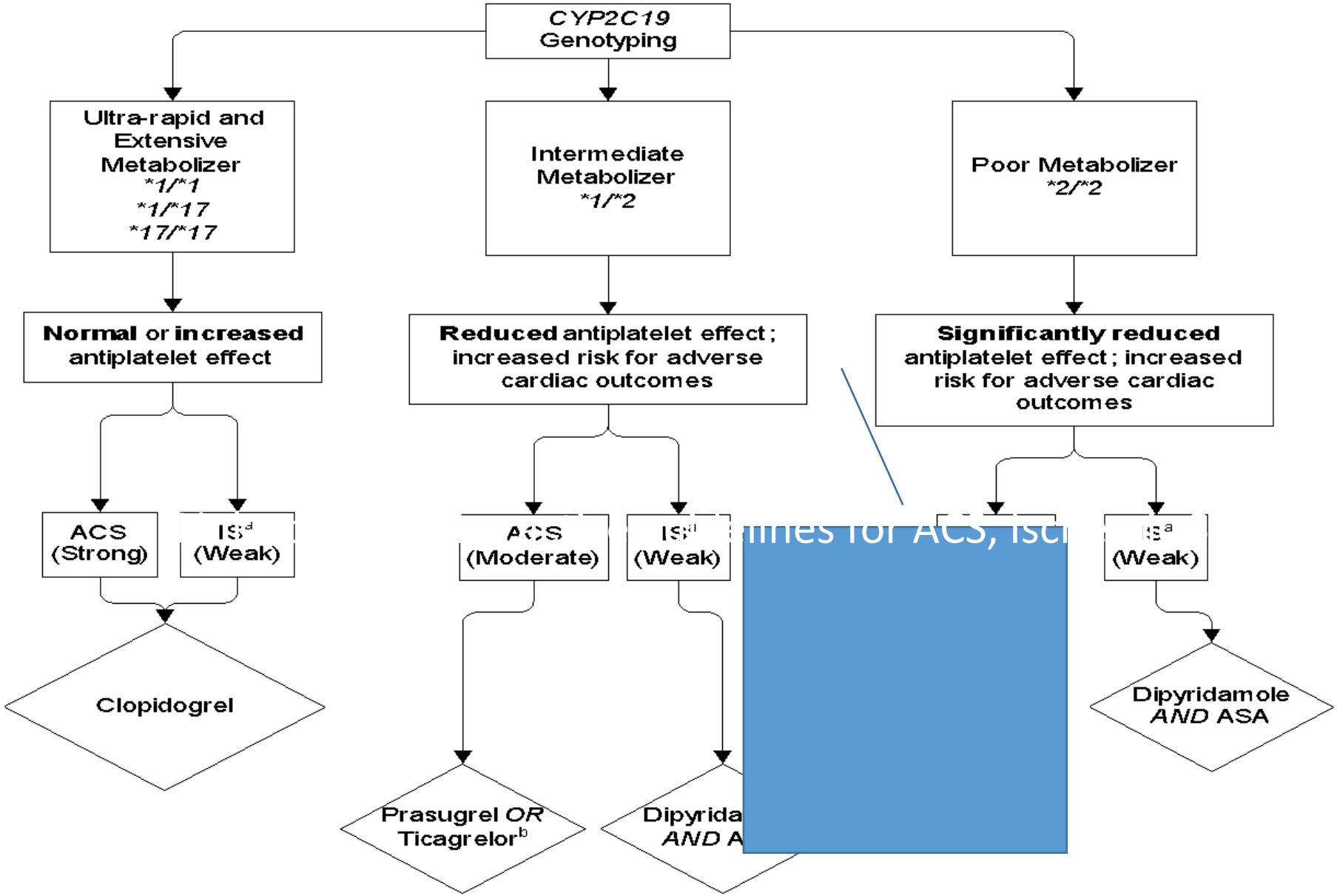
RA Wilke[1,2], LB Ramsey[3], SG Johnson[4,5], WD Maxwell[6], HL McLeod[7], D Voora[8], RM Krauss[9], DM Roden[1,2], Q Feng[1,2], RM Cooper-DeHoff[10], L Gong[11], TE Klein[11,12], M Wadelius[13] and M Niemi[14]

https://www.pharmgkb.org/page/cpic. Accessed 12/27/14

CPIC Informatics: Supporting Guideline Implementation



https://www.pharmgkb.org/page/cpicInformatics. Accessed 4/27/15



Johnson SG. KP Colorado *CYP2C19* Algorithm

American Journal of Medical Genetics Part C (Seminars in Medical Genetics) 166C:56–67 (2014)

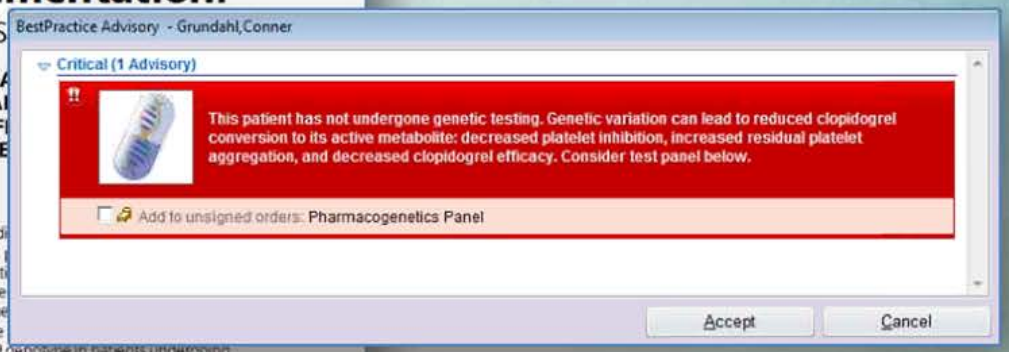
ARTICLE

Clinical Pharmacogenetics Implementation:
Approaches, Successes, and Challenges

**KRISTIN W. WEITZEL, AMANDA R. ELSEY, TAIMOUR Y. LANGA
DAVID R. NESSL, ANIWAA OWUSU OBENG, BENJAMIN J. STA
ROBERT W. ALLAN, J. FELIX LIU, RHONDA M. COOPER-DEHOF
MICHAEL CONLON, MICHAEL J. CLARE-SALZLER, DAVID R. NE**

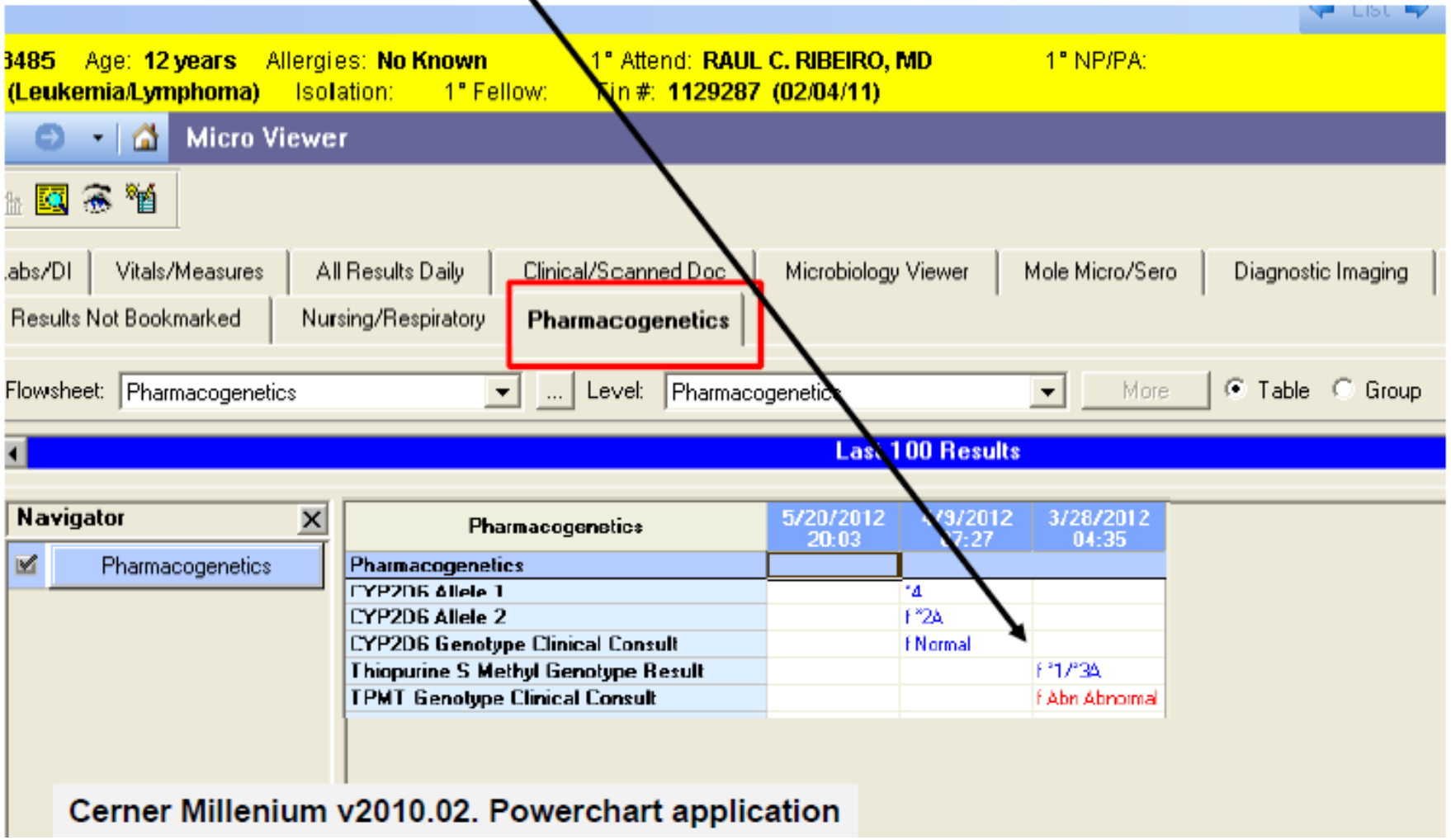
Current challenges exist to widespread clinical implementation of genomic medi
University of Florida (UF) Health Personalized Medicine Program (PMP) is a
initiative created in 2011 within the UF Clinical Translational Science Inst
pharmacogenetics, with long-term goals to include expansion to disease-risk pre
Herein we describe the processes for development of the program, the challenge
clinical acceptance by clinicians of the genomic medicine implementation. The
the UF PMP began in June 2012 and targeted clopidogrel use and the *CYP2C19* genotype in patients undergoing
left heart catheterization and percutaneous-coronary intervention (PCI). After 1 year, 1,097 patients undergoing
left heart catheterization were genotyped preemptively, and 291 of those underwent subsequent PCI. Genotype
results were reported to the medical record for 100% of genotyped patients. Eighty patients who underwent PCI
had an actionable genotype, with drug therapy changes implemented in 56 individuals. Average turnaround time
from blood draw to genotype result entry in the medical record was 3.5 business days. Seven different third party
payors, including Medicare, reimbursed for the test during the first month of billing, with an 85% reimbursement
rate for outpatient claims that were submitted in the first month. These data highlight multiple levels of success in
clinical implementation of genomic medicine.

KEY WORDS: pharmacogenetics; genomic medicine; implementation; *CYP2C19*; personalized medicine



UF
UNIVERSITY of FLORIDA

All clinical genotype results are posted in EMR



Courtesy of Clinical Pharmacogenetics Service at
St. Jude PediatricResearch Hospital

Clinical Pharmacogenomics Consult Entered into EMR

PKN Tests	
Thiopurine S Methyl Genotype Result	f *1/*3A
TPMT Genotype Clinical Consult	f Abn Abnormal

PHARMACOKINETICS CONSULT FOR
TPMT GENOTYPE

Pharmacist enters a pharmacogenomics consult into medical record

Sample for TPMT genotype obtained 06/11/12.
Thiopurine S Methyl Transferase Genotype Result: *1/*3A.

This result means the genotype is heterozygous. Heterozygous means intermediately low TPMT activity. This patient may be at risk for toxicity with 6-mercaptopurine and should receive no more than 60 mg/msq/day of 6-mercaptopurine pending further evaluation by a clinical pharmacist and attending Hematology/Oncology physician. If myelosuppression occurs, this result suggests that the 6-mercaptopurine dose be titrated based on WBC and ANC. Every effort should be made to keep other anticancer agent doses at protocol levels.

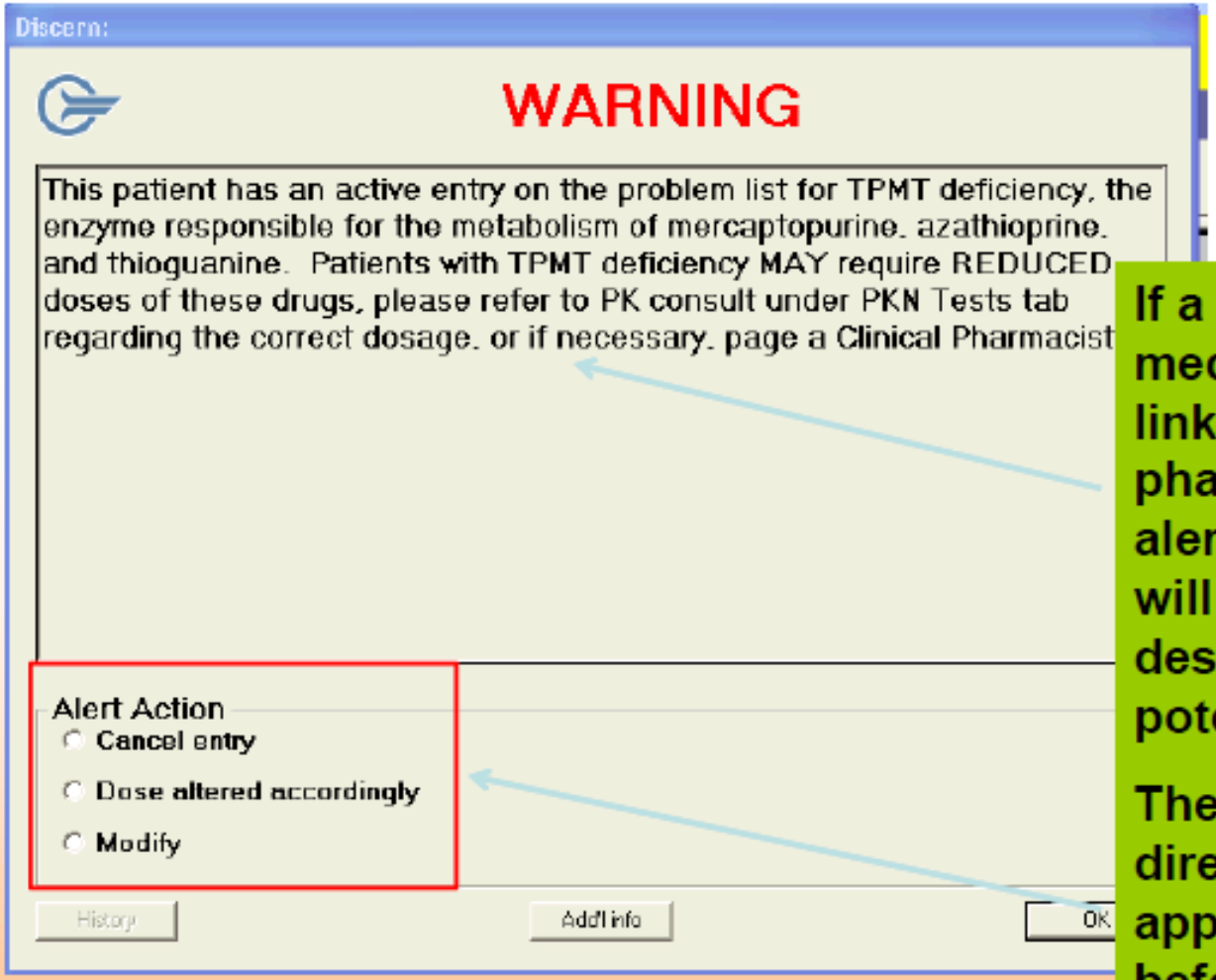
Time/date of Consult: 06/15/2012 15:18 **Jane Smith, Pharm.D.**

Management Discipline View Active Problems Change View

Annotated Display	Qualifier	Onset Date	Classification	Life Cycle Status
Medical				
ACUTE LYMPHOCYTIC LEUKEMIA		06/04/2010	HIMS Summary	Active
TPMT - Thiopurine methyltranslerase deficiency		06/11/2010	Medical	Active

Courtesy of Clinical Pharmacogenetics Service at
St. Jude PediatricResearch Hospital

Clinical Decision Support an Integral Component



If a clinician selects a medication that is linked to the pharmacogenomic alert, a Warning Box will appear with a brief description of the potential problem.

The clinician is then directed to select an appropriate action before proceeding.

Courtesy of Clinical Pharmacogenetics Service at
St. Jude PediatricResearch Hospital

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Meeting

Improving Genetics Education in Graduate and Continuing Health Professional Education: A Workshop

When: August 18, 2014 (8:30 AM Eastern)

Where: Keck Center (100) • 500 Fifth St. NW, Washington, DC 20001

Topics: Biomedical and Health Research, Public Health, Education

Activity: Roundtable on Translating Genomic-Based Research for Health

Board: Board on Health Sciences Policy

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accp
American College of Clinical Pharmacy

Integrating Pharmacogenomics into Pharmacy Practice via Medication Therapy Management

A whitepaper developed by the American Pharmacists Association.

National Human Genome Research Institute

National Institutes of Health
U.S. Department of Health and Human Services

Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC)

Emerging Roles for Pharmacists in Clinical Implementation of Pharmacogenomics

Aniwaa Owusu-Obeng,[1,2,3,†] Kristin W. Weitzel,[4,5,6,†] Randy C. Hatton,[7] Benjamin J. Staley,[7] Jennifer Ashton,[7] Rhonda M. Cooper-Dehoff,[4,5,8] and Julie A. Johnson,[4,5,6,8,*]

[1]The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; [2]Pharmacy Department, The Mount Sinai Hospital, New York, New York; [3]Division of General Internal Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; [4]UF Health Personalized Medicine Program, Gainesville, Florida; [5]Department of Pharmacotherapy and Translational Research, Center for Pharmacogenomics, College of Pharmacy, University of Florida, Gainesville, Florida; [6]Clinical & Translational Science Institute, University of Florida, Gainesville, Florida; [7]Pharmacy Department, UF Health Shands Hospital, Gainesville, Florida; [8]Department of Medicine, University of Florida, Gainesville, Florida

Pharmacists are uniquely qualified to play essential roles in the clinical implementation of pharmacogenomics. However, specific responsibilities and resources needed for these roles have not been defined. We describe roles for pharmacists that emerged in the clinical implementation of genotype-guided clopidogrel therapy in the University of Florida Health Personalized Medicine Program, summarize

B: BASIC GENETIC CONCEPTS

- B1: To demonstrate an understanding of the basic genetic/genomic concepts and nomenclature
- B2: To recognize and appreciate the role of behavioral, social, and environmental factors (lifestyle, socioeconomic factors, pollutants, etc.) to modify or influence genetics in the manifestation of disease
- B3: To identify drug and disease associated genetic variations that facilitate development of prevention, diagnostic and treatment strategies and appreciate there are differences in testing methodologies and are aware of the need to explore these differences these differences in drug literature evaluation
- B4: To use family history (minimum of three generations) in assessing predisposition to disease and selection of drug treatment

G: GENETICS AND DISEASE

- G1: To understand the role of genetic factors in maintaining health and preventing disease
- G2: To assess the difference between clinical diagnosis of disease and identification of genetic predisposition to disease (genetic variation is not strictly correlated with disease manifestation)
- G3: To appreciate that pharmacogenomic testing may also reveal certain genetic disease predispositions (e.g. the Apo E4 polymorphism)

P: PHARMACOGENETICS/PHARMACOGENOMICS

- P1: To demonstrate an understanding of how genetic variation in a large number of proteins, including drug transporters, drug metabolizing enzymes, direct protein targets of drugs, and other proteins (e.g. signal transduction proteins) influence pharmacokinetics and pharmacodynamics related to pharmacologic effect and drug response
- P2: To understand the influence (or lack thereof) of ethnicity in genetic polymorphisms and associations of polymorphisms with drug response
- P3: Recognize the availability of evidence based guidelines that synthesize information relevant to genomic/pharmacogenomic tests and selection of drug therapy (e.g. Clinical Pharmacogenomics Implementation Consortium)

E: ETHICAL, LEGAL AND SOCIAL IMPLICATIONS (ELSI)

- E1: To understand the potential physical and/or psychosocial benefits, limitations and risk of genomic/pharmacogenomic information for individuals, family members and communities, especially with genomic/pharmacogenomic tests that may relate to predisposition to disease
- E2: To understand the increased liability that accompanies access to detailed genomic patient information and maintain confidentiality and security
- E3: To adopt a culturally sensitive and ethical approach to patient counseling regarding genomic/pharmacogenomic test results
- E4: To appreciate the cost, cost-effectiveness, and reimbursement by insurers relevant to genomic or pharmacogenomic tests and test interpretation, for patients and populations
- E5: To Identify the need to refer a patient to a genetic specialist or genetic counselor

G2C2

GENETICS/GENOMICS COMPETENCY CENTER

Pharmacist Competency Map. Genetics and Genomics Competency Center. Available at: http://g-2-c-2.org/competency/pharmacist