

Genomic Medicine Working Group Update

Teri Manolio, M.D., Ph.D.

National Advisory Council on Human Genome Research
September 24, 2018



The **Forefront**
of **Genomics**

NACHGR Genomic Medicine Working Group Members

Carol Bult

Rex Chisholm

Pat Deverka

Geoff Ginsburg

Howard McLeod

George Mensah

Mary Relling

Dan Roden

Marc Williams

NHGRI

Eric Green

Teri Manolio

Laura Rodriguez

Jackson Labs

Northwestern

Am Institutes for Research

Duke

Moffitt Cancer Center

NHLBI

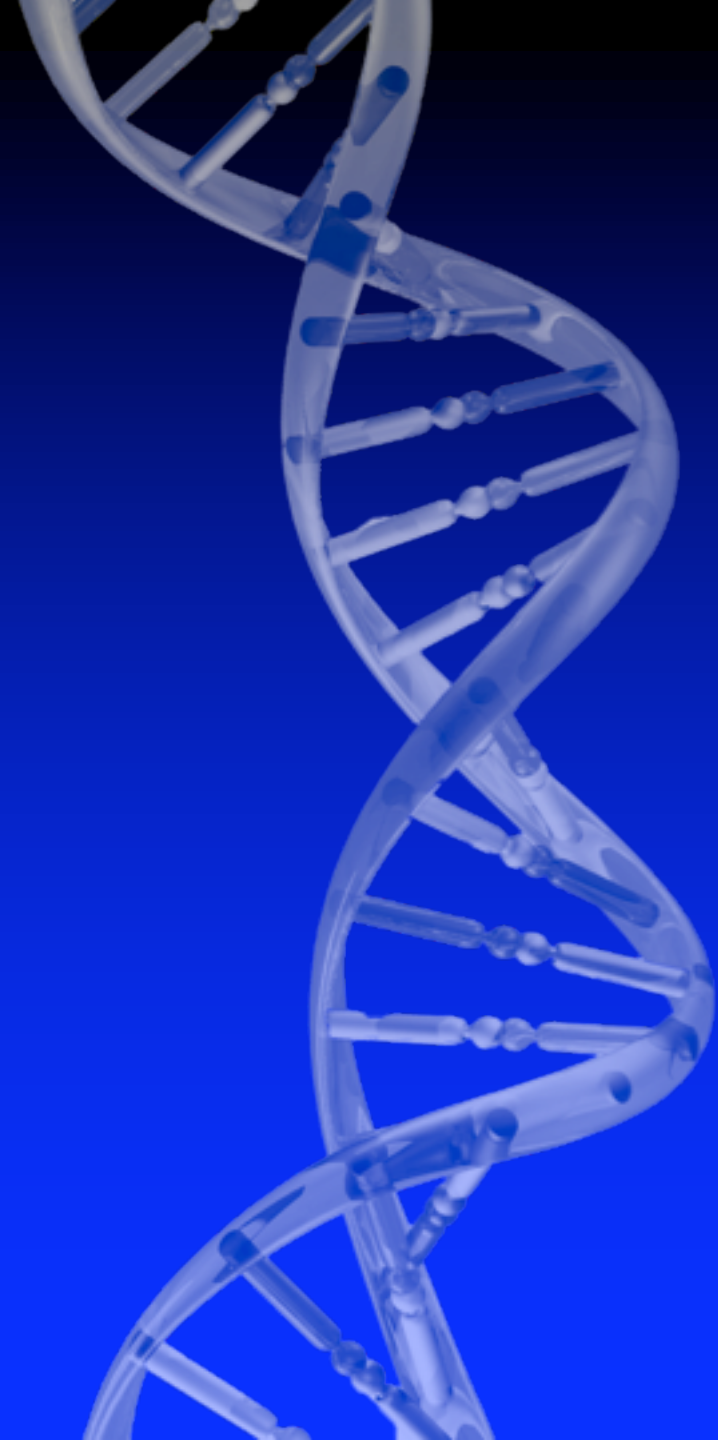
St. Jude

Vanderbilt

Geisinger

Robb Rowley

Cecelia Tamburro



Spectrum of Disease-Related Genomics Research

Genomic Medicine

Genomic Medicine Working Group Charge

Assist in advising NHGRI on research needed to evaluate and implement genomic medicine

- Review current progress, identify research gaps and approaches for filling them
- Identify and publicize key advances
- Plan genomic medicine meetings on timely themes
- Facilitate collaborations, coordination
- Explore models for long-term infrastructure and sustainability of resulting efforts



Notable Accomplishments in Genomic Medicine



National Human Genome
Research Institute

Search Genome.gov

Español



Genomic Medicine Activities

Notable Accomplishments in Genomic Medicine

nature
genetics

LETTERS

<https://doi.org/10.1038/s41588-018-0183-z>

Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations

Amit V. Khera^{1,2,3,4,5}, Mark Chaffin^{4,5}, Krishna G. Aragam^{1,2,3,4}, Mary E. Haas⁴, Carolina Roselli⁴, Seung Hoan Choi⁴, Pradeep Natarajan^{2,3,4}, Eric S. Lander⁴, Steven A. Lubitz^{2,3,4}, Patrick T. Ellinor^{2,3,4} and Sekar Kathiresan^{1,2,3,4*}

Genomic Medicine Colloquium, June 2011

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REVIEW | Genetics in Medicine

Open

Implementing genomic medicine in the clinic: the future is here

Teri A. Manolio, MD, PhD¹; Rex L. Chisholm, PhD²; Brad Ozenberger, PhD¹; Dan M. Roden, MD³; Marc S. Williams, MD^{4,5}; Richard Wilson, PhD⁶; David Bick, MD⁷; Erwin P. Bottinger, MD⁸; Murray H. Brilliant, PhD⁹; Charis Eng, MD, PhD¹⁰; Kelly A. Frazer, PhD¹¹; Bruce Korf, MD, PhD¹²; David H. Ledbetter, PhD⁵; James R. Lupski, MD, PhD¹³; Clay Marsh, MD¹⁴; David Mrazek, MD¹⁵; Michael F. Murray, MD¹⁶; Peter H. O'Donnell, MD¹⁷; Daniel J. Rader, MD¹⁸; Mary V. Relling, PharmD¹⁹; Alan R. Shuldiner, MD²⁰; David Valle, MD²¹; Richard Weinshtaub, MD²²; Eric D. Green, MD, PhD¹ and Geoffrey S. Ginsburg, MD, PhD²³

Although the potential for genomics to contribute to clinical care has long been anticipated, the pace of defining the risks and benefits of incorporating genomic findings into medical practice has been

ndent, lack of reimbursement for genomically driven interventions, and burden to patients and clinicians of assaying, reporting, interpreting, and following up genomic findings. Key infrastructure needs

GM II: Forming Collaborations, Dec 2011

metree™

Welcome to MeTree. This program will ask questions about your health and your family's health. Your answers will be used to give you personalized suggestions for your health care. Please answer as best you can.

TOUCH HERE TO START

GM III: Stakeholders, May 2012

Technology Assessment Supports Health Plans and Other Stakeholders in Developing Evidence-based Policies

Medical Policy | Coverage Policy | Payment Policy

GM IV: Physician Education, Jan 2013



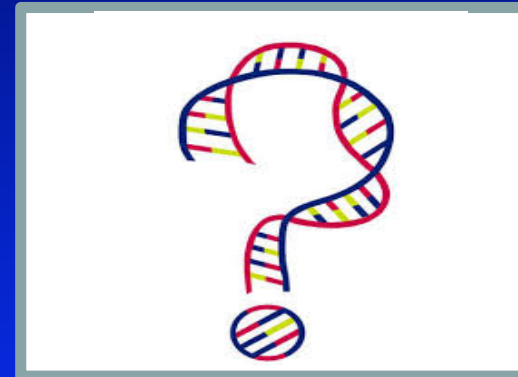
GM X: PGx Implementation, May 2017



GM XI: Clinical Implementation, Sept 2018



GM XII:



GM V: Federal Strategies, May 2013

cap

A Genomic Medicine Policy Framework

The College of American Pathologists
Debra G.B. Leonard, MD, PhD, FCAP

GM IX: Bedside Back to Bench, April 2016



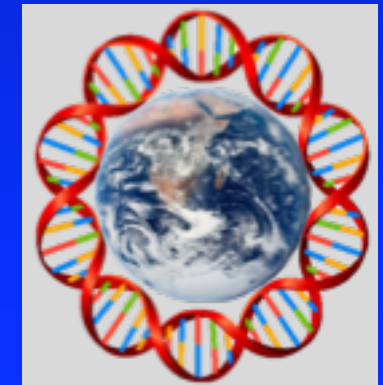
GM VIII: NHGRI's Genomic Medicine Programs, June 2015




GM VII: Genomic CDS, Oct 2014



GM VI: Global Leaders, Jan 2014



Genomic Medicine Meetings


National Human Genome Research Institute

Genomic Medicine Meetings

NHGRI held a series of meetings that have been involved with the implementation of genomic medicine; sharing best practices and opportunities; sharing research findings; and exploring possible collaborative opportunities.

- **Genomic Medicine X: Research Directions in Pharmacogenomics Implementation** September 5-6, 2017, La Jolla, California
- **Genomic Medicine IX: Research Directions in Pharmacogenomics Implementation** May 2-3, 2017, Silver Spring, Maryland
- **Genomic Medicine VIII: Research Directions in Pharmacogenomics Implementation** April 19-20, 2016, San Francisco, California
- **Genomic Medicine VII: Research Directions in Pharmacogenomics Implementation** June 8-9, 2015, Rockville, Maryland
- **Genomic Medicine VI: Research Directions in Pharmacogenomics Implementation** October 2-3, 2014, Silver Spring, Maryland
- **Genomic Medicine V: Research Directions in Pharmacogenomics Implementation** January 8-9, 2014, Silver Spring, Maryland


Genomic Medicine Activities

- Genomic Medicine II
- Genomic Medicine III
- Genomic Medicine IV

On September 5-6, 2017, the National Human Genome Research Institute (NHGRI) sponsored its 10th Genomic Medicine meeting - *Genomic Medicine X: Research Directions in Pharmacogenomics Implementation* - at the Sheraton Silver Spring Hotel in Silver Spring, Maryland.

Wednesday, September 6, 2017

Time	Topic
8:30 a.m.	Welcome
8:45 a.m.	Overview



On May 2-3, 2017, the National Human Genome Research Institute (NHGRI) sponsored its 10th Genomic Medicine meeting - *Genomic Medicine X: Research Directions in Pharmacogenomics Implementation* - at the Sheraton Silver Spring Hotel in Silver Spring, Maryland.

The objectives of the meeting were to:

- Survey national landscape of research programs in pharmacogenomics implementation
- Review current advances and clinical applications of pharmacogenomics

- Discuss limitations and obstacles in pharmacogenomics clinical implementation
- Identify evidence gaps and studies that are needed to address them
- Design strategies for large-scale evaluation and implementation of pharmacogenomics in clinical care in the United States.

[YouTube Video Playlist: Genomic Medicine X: Pharmacogenomics](#)

- [Meeting Summary](#)
- [Executive Summary](#)
- [Tweets from the meeting: #GenomicMed10](#)
- [GOLDILOKs Study: Patient Booklet](#)

Tuesday, May 2, 2017

Time	Topic	Speaker
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GMWG Publications

Genetics

American Journal of Medical Genetics Part C (Seminars in Medical Genetics) 166C:93-104 (2014)

ARTICLE

Open

Genetics

Sci Transl Med 2015; 7:290ps13.

PERSPECTIVE

POLICY

Global
We are

Cell

Teri A. Manolio¹,
Rudi Balling²,
Chantratita
Victor J. Dzau³,
Michiaki Kubo⁴,
Partha P. Mitra⁵,
Pierre Morel⁶,
George P. Patrino⁷,
Lyman Rodan⁸,
Patrick Tan⁹,
Wong⁴⁰ Eric

Around the world, genetic
variations arising from
undetected risk alleles
impairing of appropriate
Research Institute

Recent identification of
genetic variants for
metabolic syndrome,
therapy, and improved
treatment of declining
clinical care in
genomic medicine
only delays

Dr. Erin R...
(NHGRI). She
was the lead

Although
has long
of inco

Research Directions in the Clinical Implementation of Pharmacogenomics: An Overview of US Programs and Projects

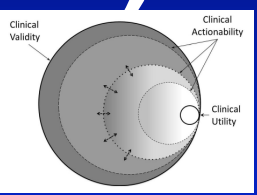
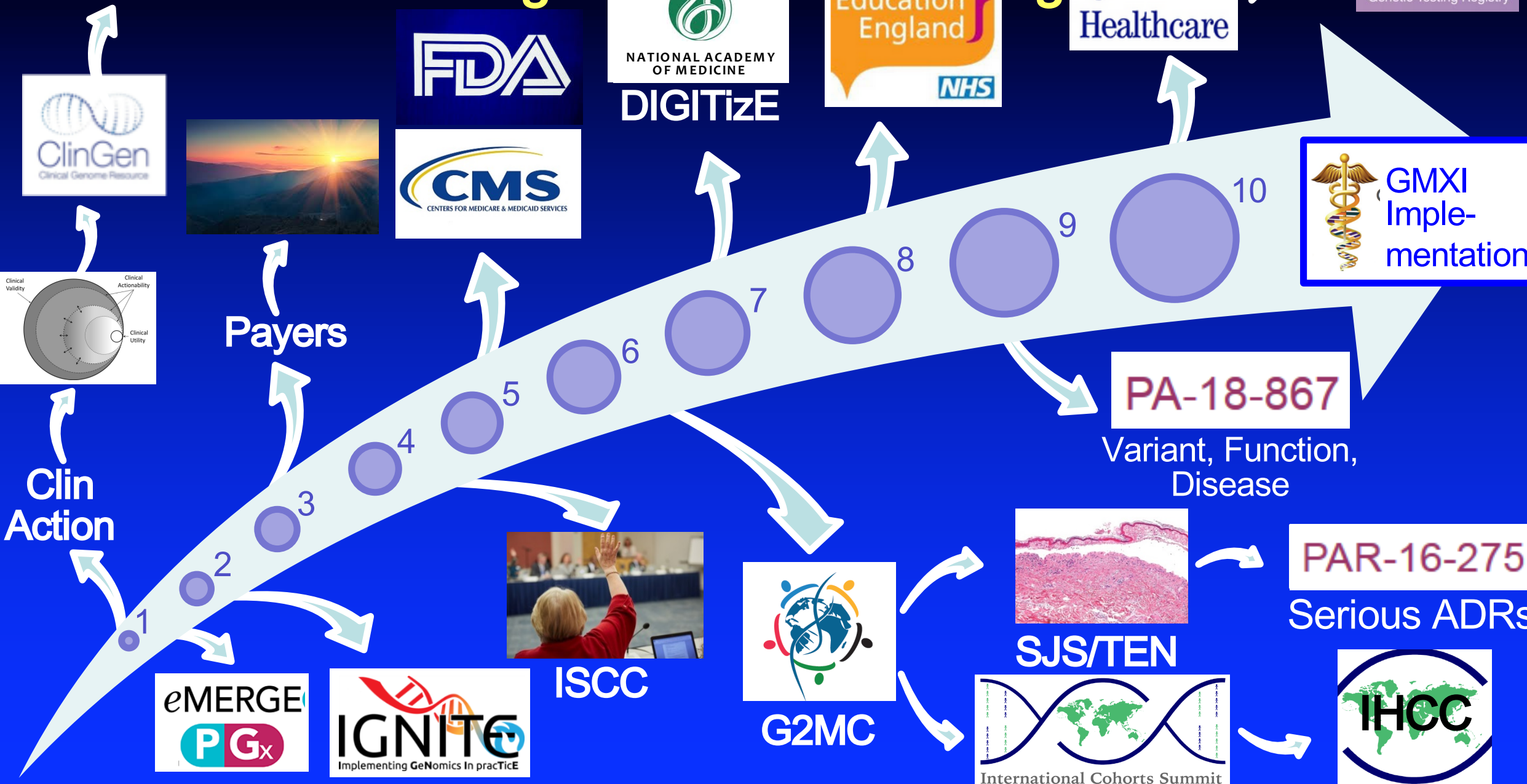
Simona Volpi¹, Carol J. Bult², Rex L. Chisholm³, Patricia A. Deverka⁴, Geoffrey S. Ginsburg⁵, Howard J. Jacob⁶, Melpomeni Kasapi¹, Howard L. McLeod⁷, Dan M. Roden⁸, Marc S. Williams⁹, Eric D. Green¹, Laura Lyman Rodriguez¹, Samuel Aronson¹⁰, Larisa H. Cavallari¹¹, Joshua C. Denny¹², Lynn G. Dressler¹³, Julie A. Johnson¹¹, Teri E. Klein¹⁴, J. Steven Leeder¹⁵, Micheline Piquette-Miller¹⁶, Minoli Perera¹⁷, Laura J. Rasmussen-Torvik¹⁸, Heidi L. Rehm¹⁹, Marylyn D. Ritchie²⁰, Todd C. Skaar²¹, Nikhil Wagle²², Richard Weinshilboum²³, Kristin W. Weitzel²⁴, Robert Wildin²⁵, John Wilson²⁶, Teri A. Manolio¹ and Mary V. Relling²⁷

Clin Pharmacol Ther 2018;103:778-86.

Response to a drug often differs widely among individual patients. This variability is frequently observed not only with respect to effective responses but also with adverse drug reactions. Matching patients to the drugs that are most likely to be effective and least likely to cause harm is the goal of effective therapeutics. Pharmacogenomics (PGx) holds the promise of precision medicine through elucidating the genetic determinants responsible for pharmacological outcomes and using them to guide drug selection and dosing. Here we survey the US landscape of research programs in PGx implementation, review current advances and clinical applications of PGx, summarize the obstacles that have hindered PGx implementation, and identify the critical knowledge gaps and possible studies needed to help to address them.

precisionFDA

Outgrowth of Genomics



Clin Action

Payers

eMERGE
PGx

IGNITE
Implementing GeNomics In practiCE

ISCC

G2MC

SJS/TEN

International Cohorts Summit

IHCC

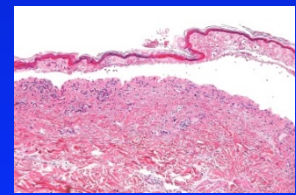
PA-18-867

Variant, Function, Disease

PAR-16-275

Serious ADRs

GMXI Implementation



CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

FDA

NATIONAL ACADEMY OF MEDICINE
DIGITIZE

Health Education England
NHS

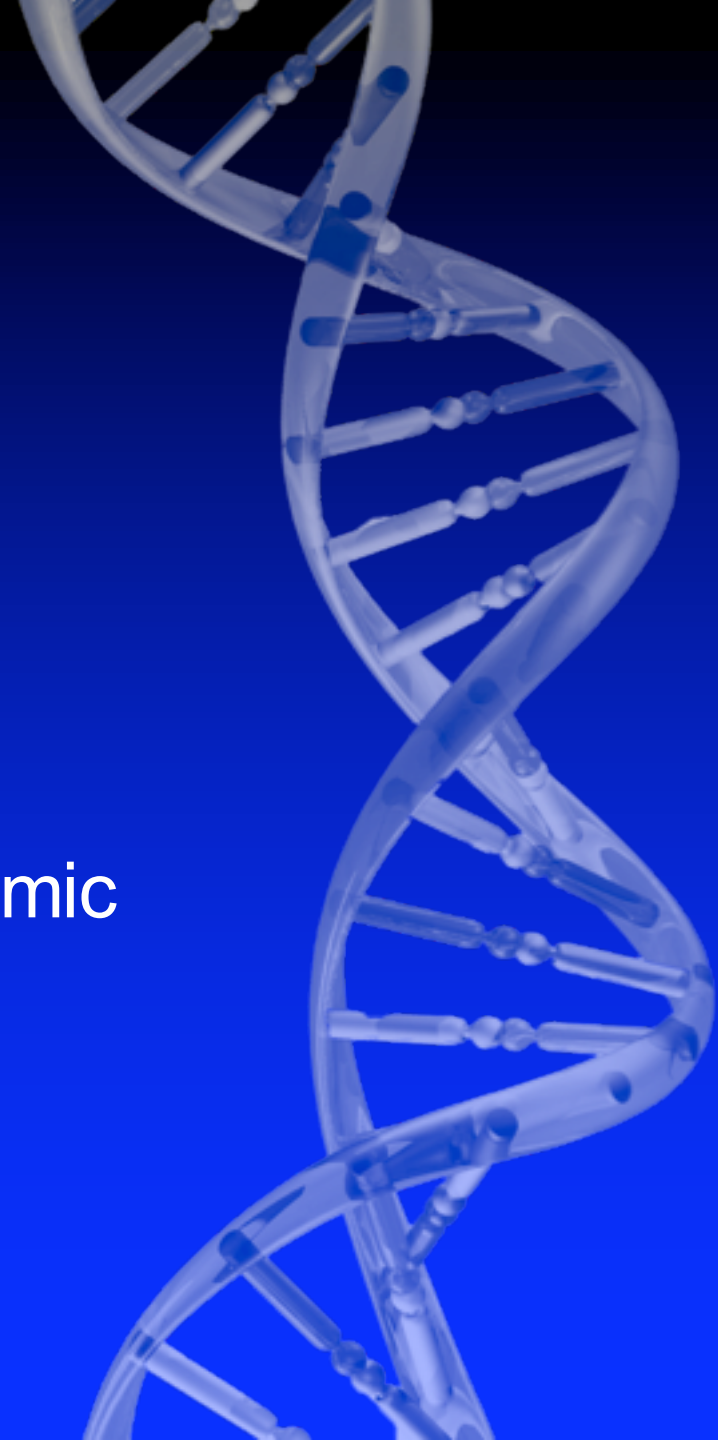
United Healthcare

GTR
Genetic Testing Registry

GM XI: Research Directions in Genomic Medicine Implementation

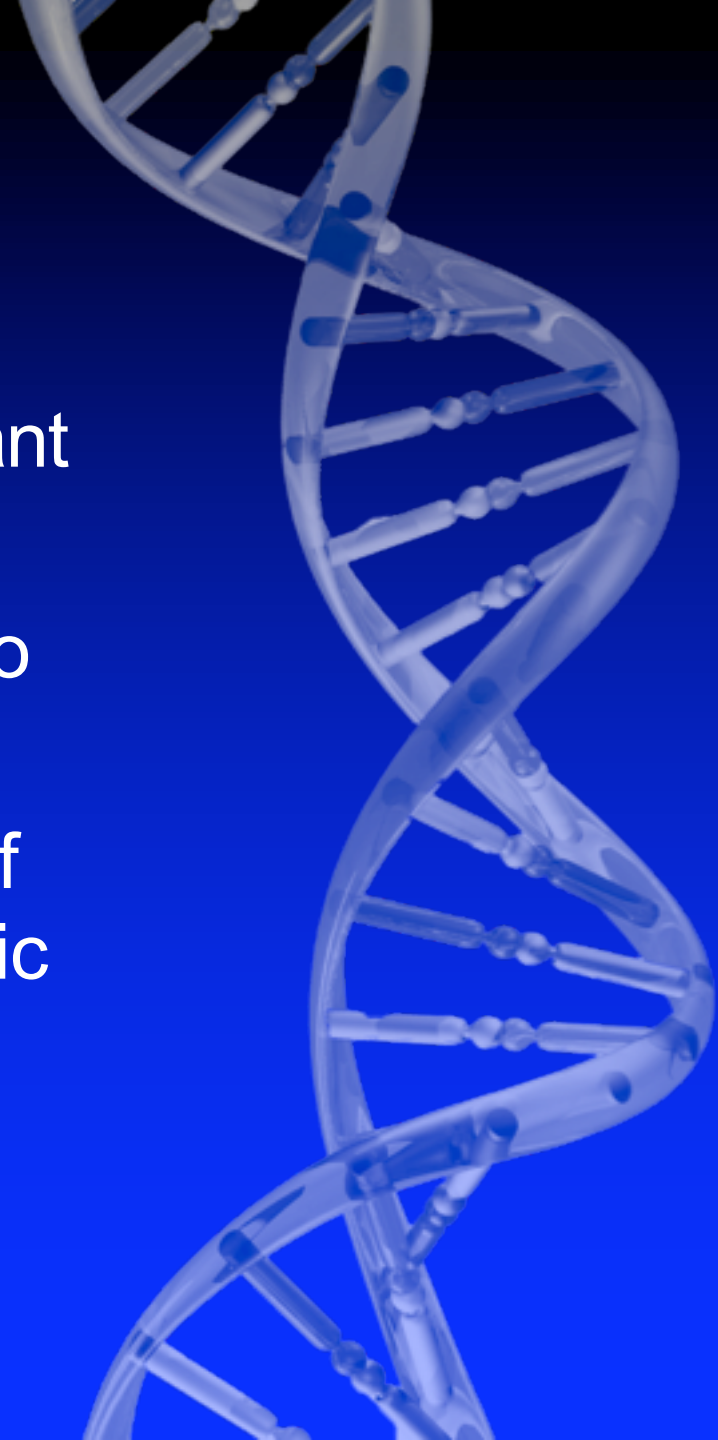
Objectives:

- Summarize the current status of genomic medicine implementation research.
- Identify obstacles to genomic medicine implementation and how to overcome them.
- Define where clinical implementation of genomic medicine could or should be 5-10 years from now and how to get there.
- Inform NHGRI strategic planning process regarding genomic medicine.



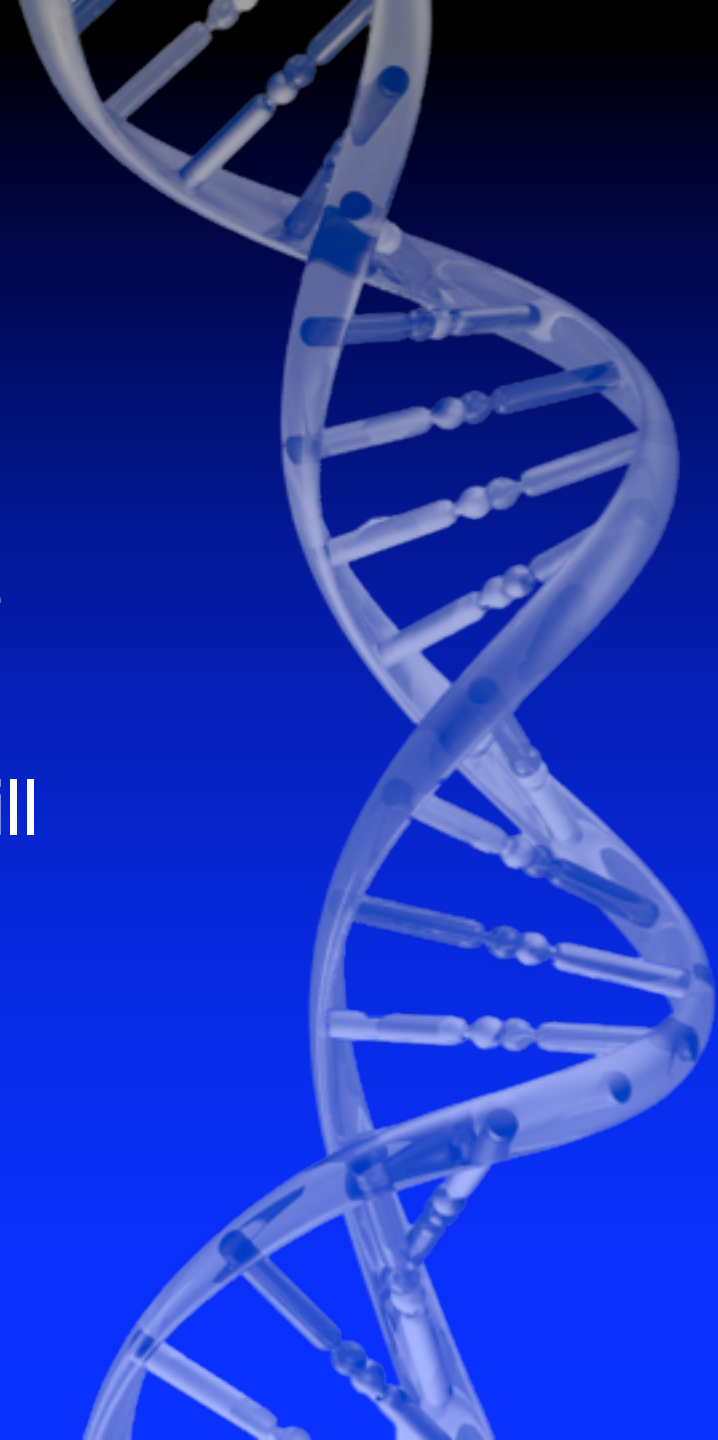
GM XI Meeting Recommendations

- Establish “CPIC”-style guideline development process for non-PGx genomic-medicine relevant genes
- Create registry of patients with genomic data to follow for outcomes
- Develop limited training program for majority of common, complex disorders; certify as genomic consultants
- Engage employers as key stakeholders



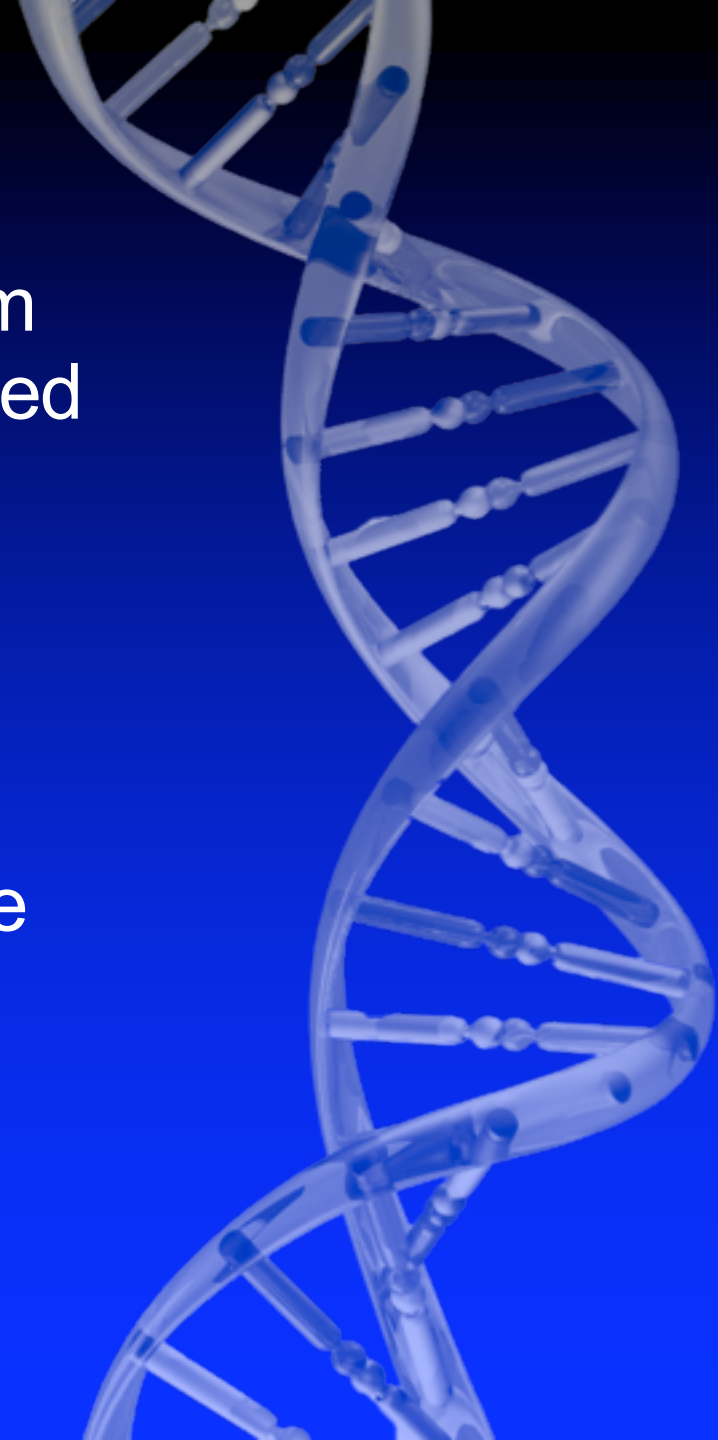
Panel: What evidence is needed?

- Evidence exists, don't be held hostage by “not enough evidence”; get on with it
- Employers may have lower threshold than payers; consumers/employees are going to be important drivers
- Employers in the service of their employees will be an important force in moving genomic medicine forward
- Reduce emphasis on educating everyone involved
- Provide consulting help on ground



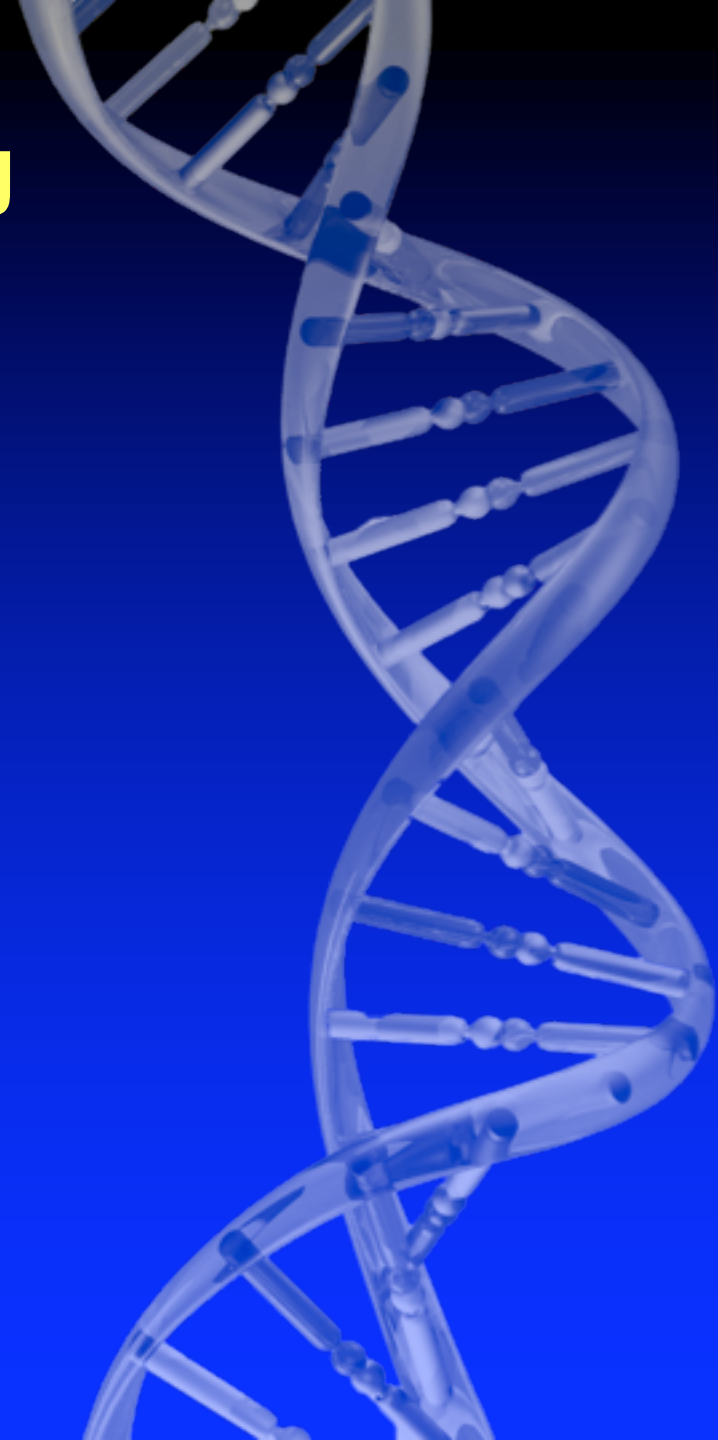
Panel: What evidence is needed?

- Need research showing employers benefit from adoption; better utilize evidence being generated even if imperfect
- Convene a group of employers and work with them to ensure rolling out in way evidence captured and publishable
- Employers self-aggregating into consortia, take advantage of this for research
- Need to develop a basic genomics formulary
- Public payers still major tough nut to crack



Employers' Genomic Medicine Meeting

- Determine employers' needs for basic and enhanced genetic testing formulary and employee health program and develop them
- Explore potential project to deploy formulary-based program within employer health plan populations and measure and publish clinical and health economic impact
- Explore additional collaborative opportunities involving pooling data from employers' health data systems to assess impact



Many Thanks...

Joy Boyer
Lisa Brooks
Heather Colley
Erin Currey
Alvaro Encinas
Eric Green
Sarah Gould
Jyoti Gupta
Lucia Hindorff
Jean Jenkins
Sheethal Jose
Dave Kaufman
Rongling Li
Nicole Lockhart
Ebony Madden

Ebony Madden
Donna Messersmith
Kiara Palmer
Erin Ramos
Robb Rowley
Laura Rodriguez
Cecelia Tamburro
Simona Volpi
Ken Wiley
Anastasia Wise
Carol Bult, Rex Chisholm,
Pat Deverka, Geoff Ginsburg,
Howard McLeod, George
Mensah, Mary Relling, Dan
Roden, Marc Williams



