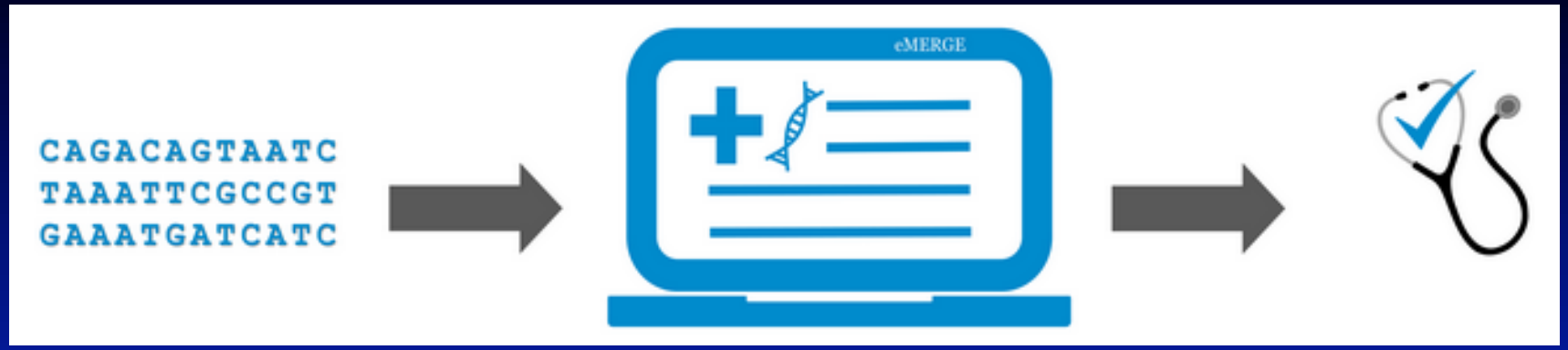


Genomic Medicine Working Group Update

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

February 10, 2020

National Human Genome Research Institute

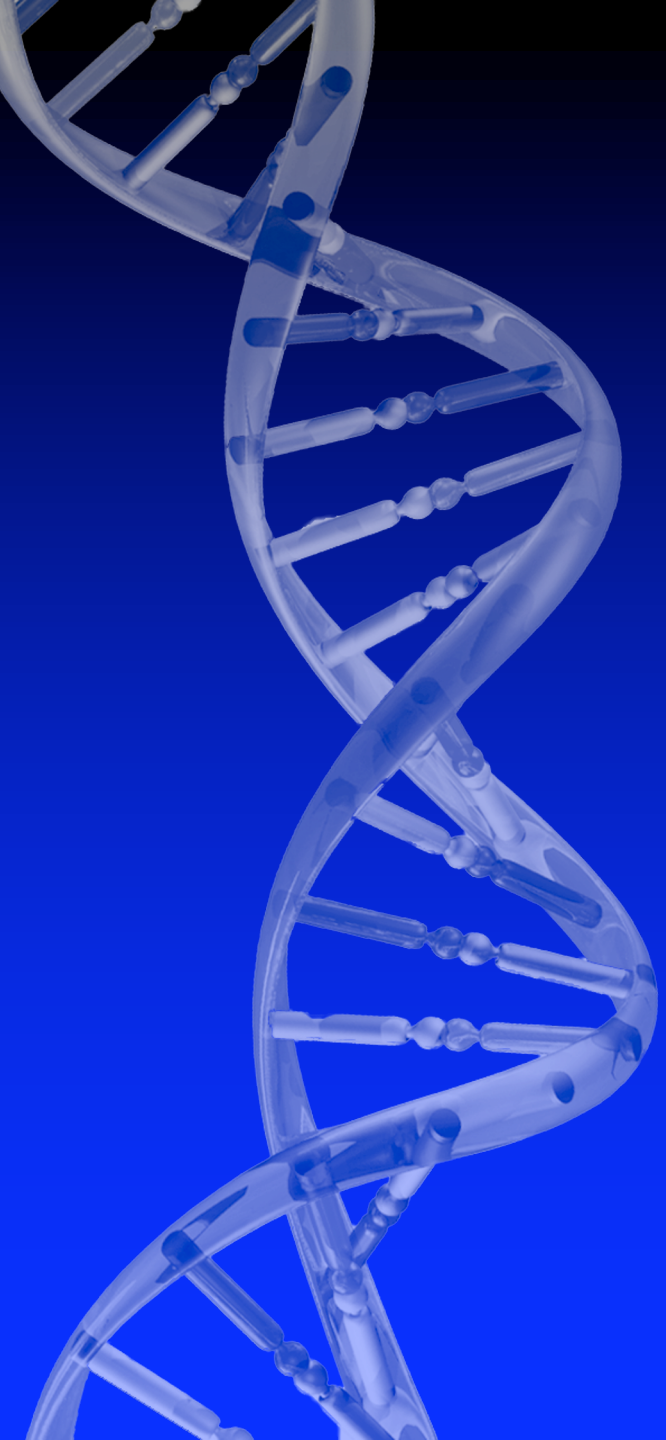
The Forefront of Genomics®

NACHGR Genomic Medicine Working Group Members

Carol Bult	Jackson Labs
Rex Chisholm	Northwestern
Pat Deverka	Innovation and Value Initiative
Geoff Ginsburg	Duke
Gail Jarvik	U Washington
George Mensah	NHLBI
Mary Relling	St. Jude
Dan Roden	Vanderbilt
Marc Williams	Geisinger

NHGRI

Eric Green	Robb Rowley
Teri Manolio	Cecelia Tamburro



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 for genomic medicine implementation

National Human Genome Research Institute

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JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 74, NO. 21, 2019

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PUBLISHED

ORIGINAL INVESTIGATIONS

Genomic Risk Prediction of Coronary Artery Disease in 480,000 Adults

Implications for Primary Prevention

Rar

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Amit V. K

Martin J.

Seyedeh

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Pharmacogenomics 2019

Clinical Implementation 2019

Sequencing 2019

Oncology 2019

Professional Guidelines and Policy 2019

November: **Diagnostic gene sequencing panels: from design**

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Gail P
Robb

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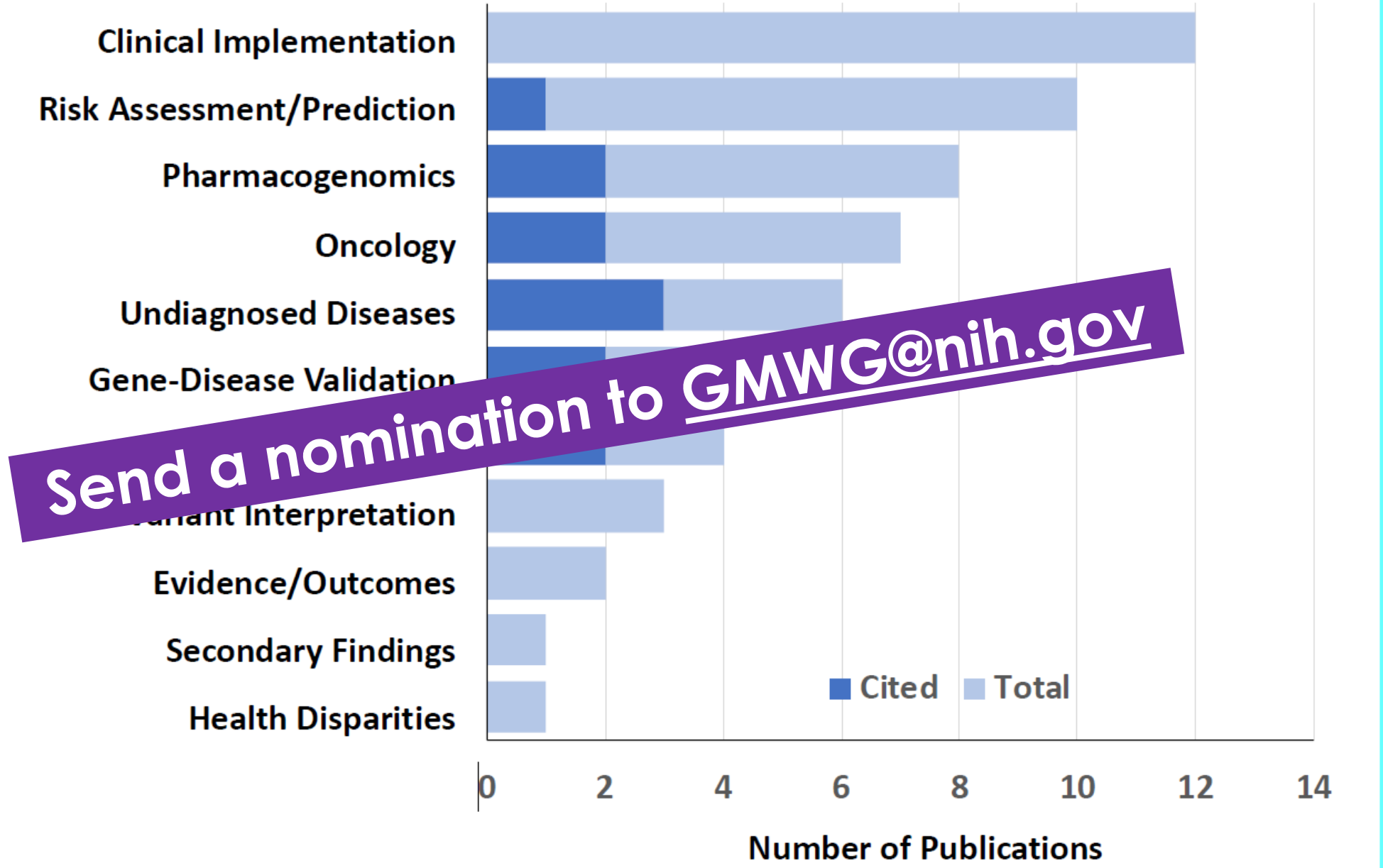

Send a nomination to GMWG@nih.gov

Am J Hum Genet 2019; 105:1072-75.

Lancet Genomic Medicine Series

Genomic Medicine 1

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Teri A Mc
George A

Genomic Medicine 2

Phar

Dan M Roc

Genomic Medicine 3

Genc

Anastasia L

Genomic Medicine 4

Fami
asses

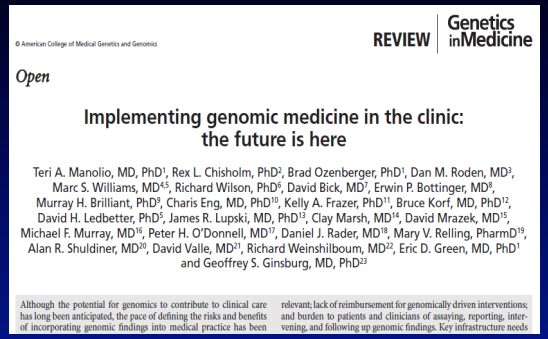
Geoffrey S G

Genomic Medicine 5

Building evidence and measuring clinical outcomes for genomic medicine

Josh F Peterson, Dan M Roden, Lori A Orlando, Andrea H Ramirez, George A Mensah, Marc S Williams

Genomic Medicine Colloquium, June 2011

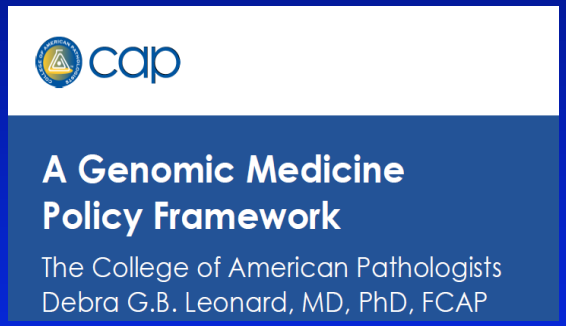


GM II: Forming Collaborations, Dec 2011

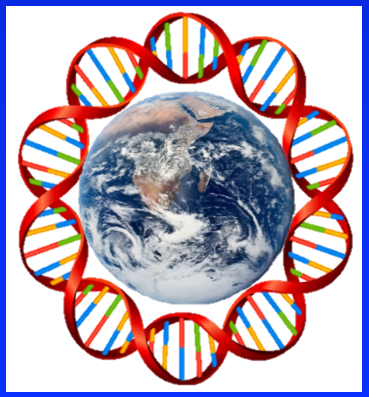
GM III: Stakeholders, May 2012

GM IV: Physician Education, Jan 2013

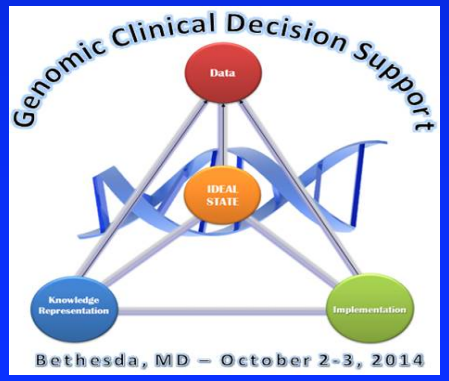
GM V: Federal Strategies, May 2013



GM VI: Global Leaders, Jan 2014



GM VII: Genomic CDS, Oct 2014



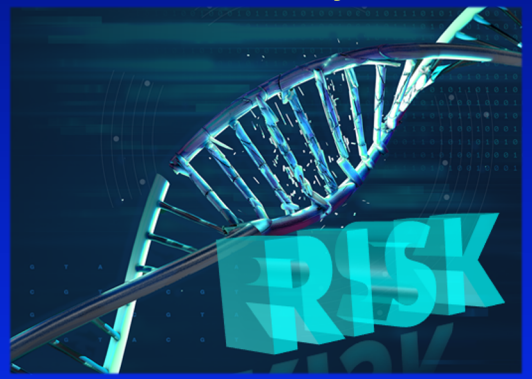
GM VIII: NHGRI's Genomic Medicine Programs, June 2015

GM IX: Bedside Back to Bench, April 2016

GM X: PGx Implementation, May 2017

GM XI: Clinical Implementation, Sept 2018

GM XII: Genomics and Risk Prediction, May 2019



Outgrowths of GM Meeting

precisionFDA

GenomeConnect
The ClinGen Patient Portal

ClinGen
Clinical Genome Resource

Clin Action

Payers

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

The National Academies of SCIENCES ENGINEERING MEDICINE
ACTION COLLABORATIVES
DIGITizE: Displaying and Integrating Genetic Information Through the EHR

DIGITizE

PA-18-867

Variant, Function, Disease

Employers Health and Wellness

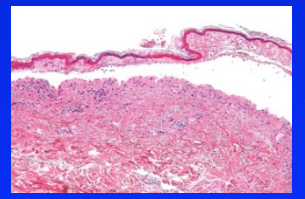
1 2 3 4 5 6 7 8 9 10 11

ISCC

Health Education England
NHS

United Healthcare

GTR
Genetic Testing Registry



SJS/TEN

PAR-16-275

Serious ADRs

eMERGE
PGx

IGNITE
Implementing GeNomics In pracTicE

G2MC

International Cohorts Summit

IHCC

GMWG Publications

Genetics

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

Genetics

PERSPECTIVE

Sci Transl Med 2015; 7:290ps13.

POLICY

Cell

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

Simona Volpi[1], Carol J. Bult[2], Rex L. Chisholm[3], Patricia A. Deverka[4], Geoffrey S. Ginsburg[5], Howard J. Jacob[6], Melpomeni Kasapi[1], Howard L. McLeod[7], Dan M. Roden[8], Marc S. Williams[9], Eric D. Green[1], Laura Lyman Rodriguez[1], Samuel Aronson[10], Larisa H. Cavallari[11], Joshua C. Denny[12], Lynn G. Dressler[13], Julie A. Johnson[11], Teri E. Klein[14], J. Steven Leeder[15], Micheline Piquette-Miller[16], Minoli Perera[17], Laura J. Rasmussen-Torvik[18], Heidi L. Rehm[19], Marylin D. Ritchie[20], Todd C. Skaar[21], Nikhil Wagle[22], Richard Weinshilboum[23], Kristin W. Weitzel[24], Robert Wildin[25], John Wilson[26], Teri A. Manolio[1] and Mary V. Relling[27]

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.

Genomic Medicine Meetings

NIH National Human Genome Research Institute

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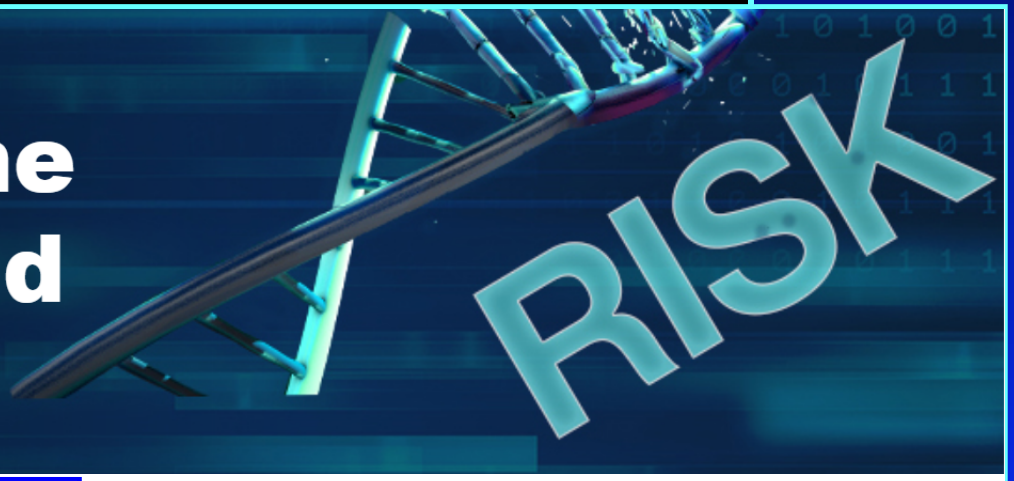
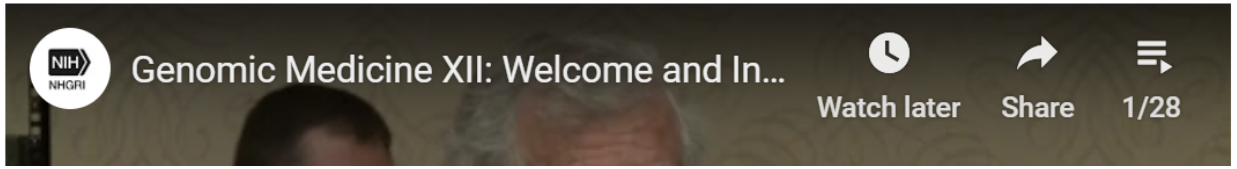
Genomic Medicine XII: Genomics and Risk Prediction



Agenda

Executive Summary
Meeting Summary

8:30 a.m. Welcome and Introductions
Teri Manolio, Dan Roden

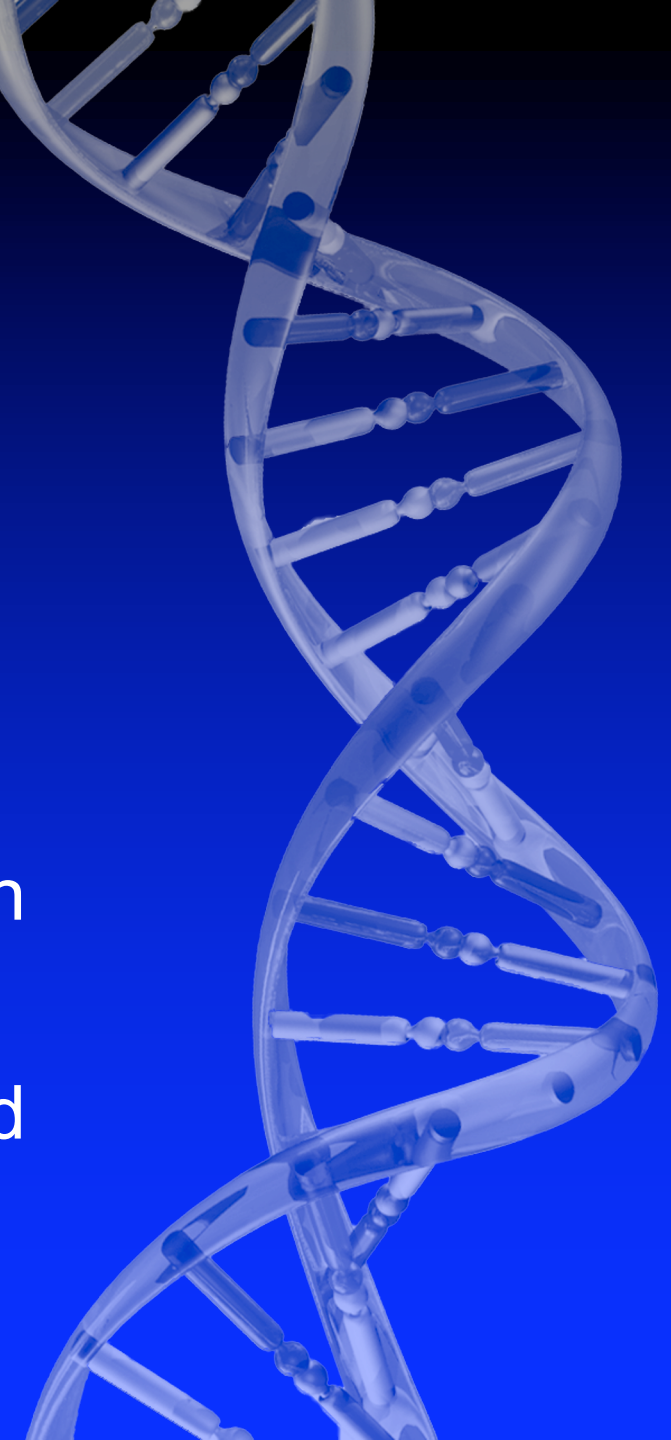


Video (Roden) - Video (Manolio) - Slides

GM XII: Research Directions in Genomic Medicine Implementation, May 6-7, 2019

Objectives:

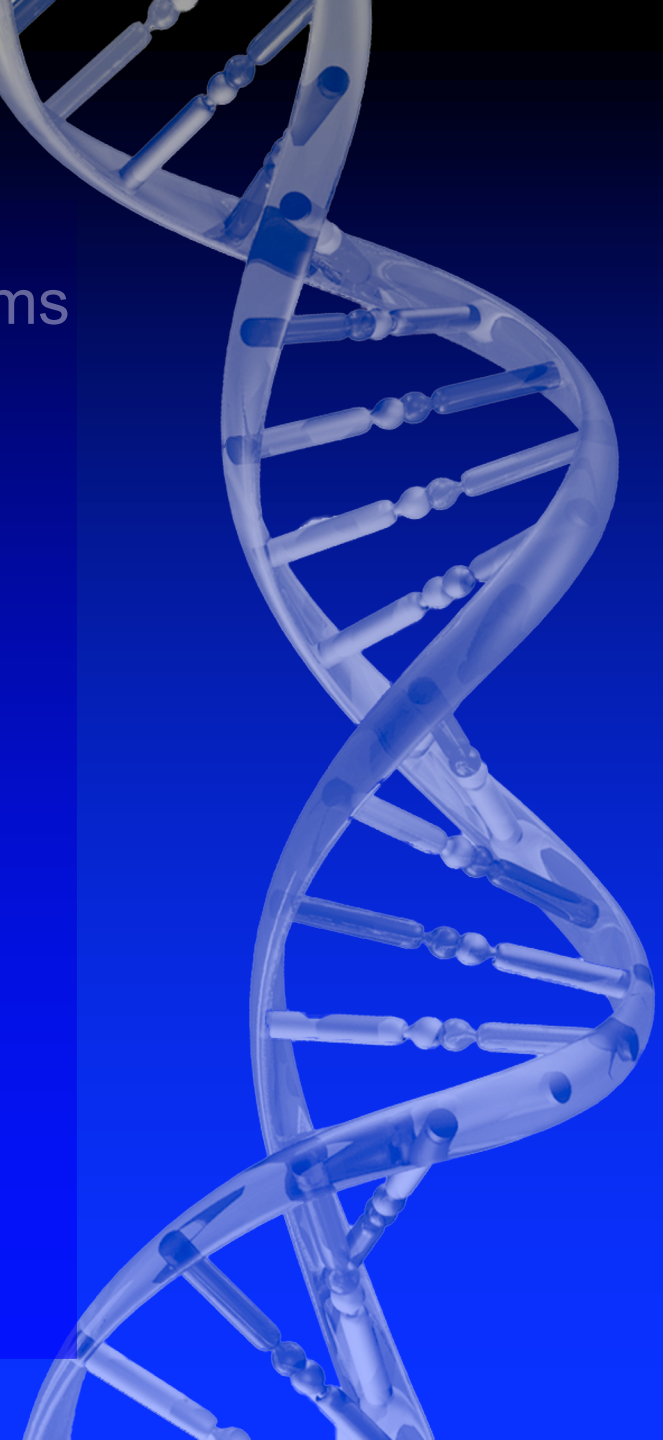
- Review the state of science of polygenic risk scores and how it can be improved
- Examine other information sources that should be integrated with genetic variant information in predicting risk
- Identify research directions in development and implementation of genomic risk prediction



GM XII Meeting Recommendations

- Investigate how to accelerate adoption of evidence-based risk prediction from early adopting centers to diverse systems
- Research best ways to communicate risk to patients and whether and how patients will want to receive risk results
- Research best ways to [illegible]s
- [illegible]
- Find ways to incorporate PRS into existing risk estimation tools to improve and speed acceptance into professional societies' guidelines
- Measure process outcomes and intermediate phenotypes related to clinical outcomes to increase PRS predictability

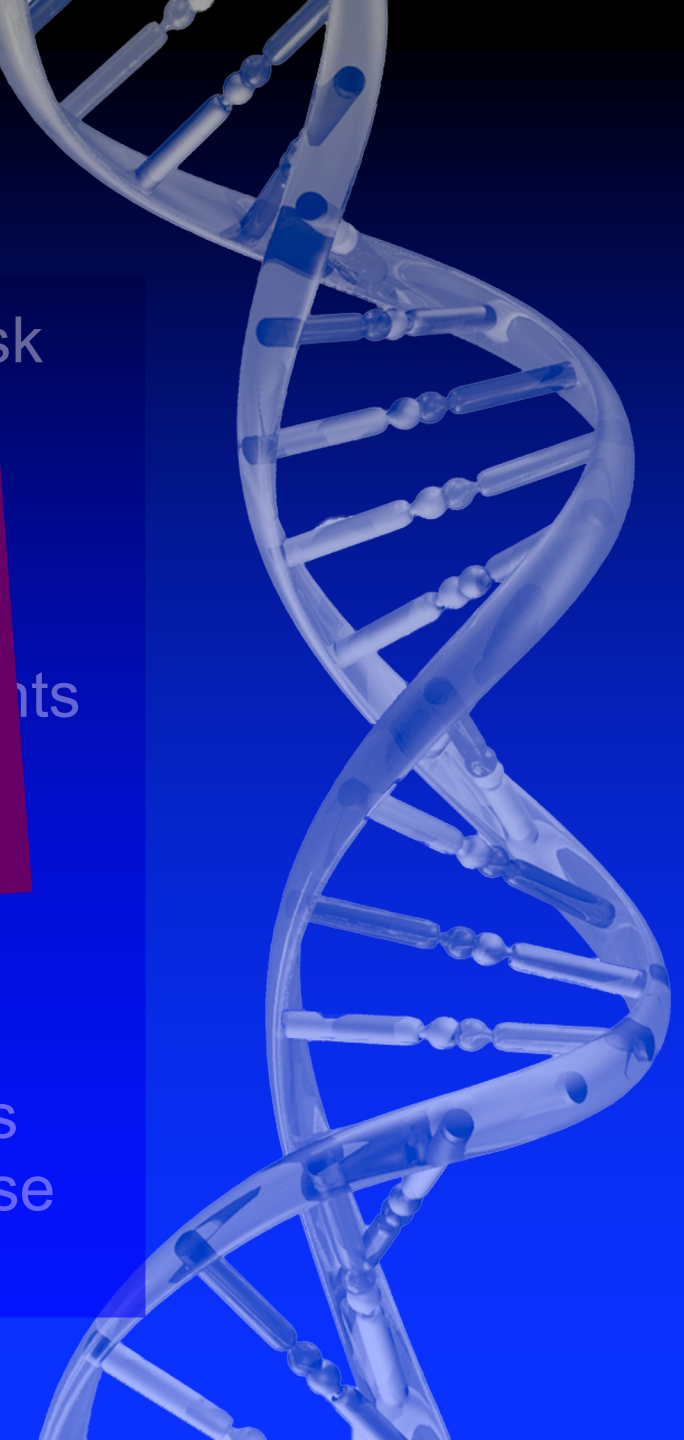
eMERGE RFAs (RFA-HG-19-013, -014, -015) will use EMRs to develop, evaluate, and disseminate genomic risk assessment and management tools for clinical use, and will validate existing PRS in diverse populations



GM XII Meeting Recommendations

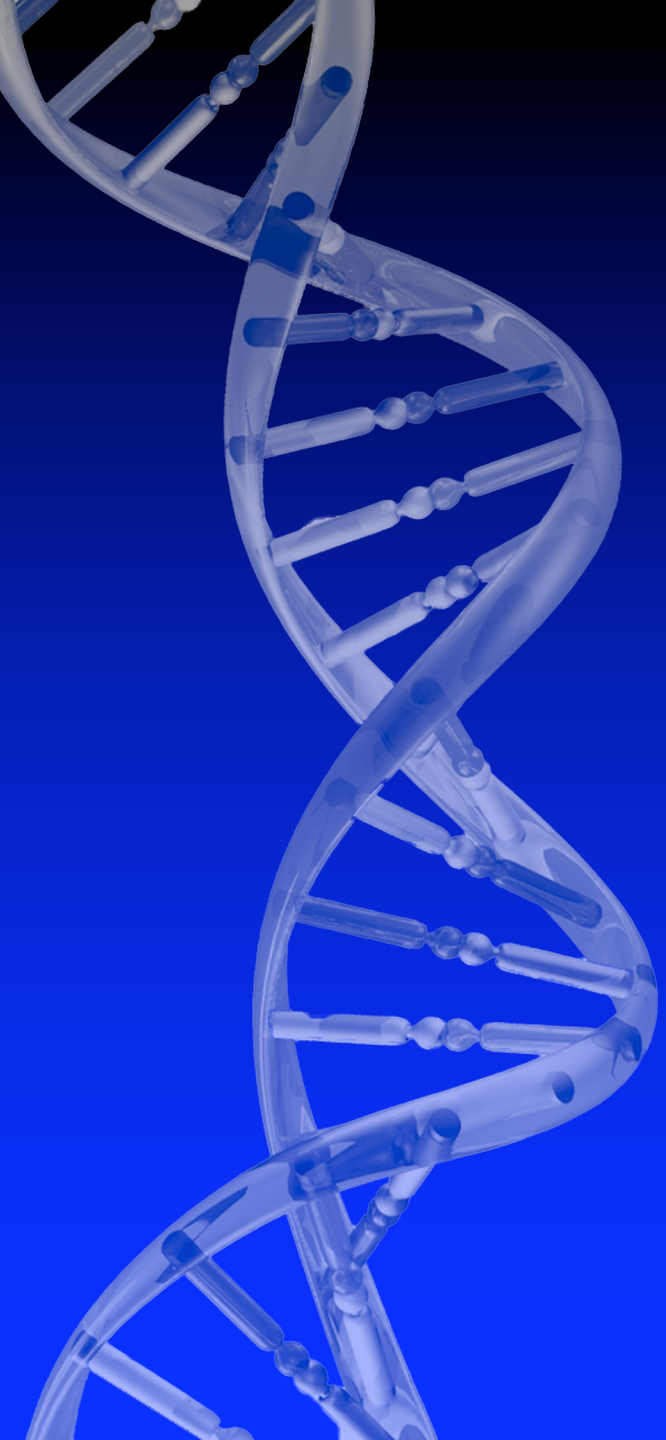
- Investigate methods for integrating other ‘omic data into risk prediction, potentially using ‘omic data as a way to weight SNP-based risk scores
- [illegible]
- [illegible]
- Develop PRS for specific disease subtypes; a “one size fits all” approach does not always work when predicting disease risk, especially in non-EA populations

NOT-HG-20-010, “Development of Statistical, Population Genetics and Computational Methods Related to Polygenic Prediction of Health and Disease in Diverse Populations,” encourages investigation into novel ‘omic methods, heterogeneity across populations, and modeling differences in risk prediction across subgroups



Panel on Multi-Condition PRS Studies: Capture Breadth of Conditions

- Disease incidence, risk variants, risk magnitudes across different ancestries
- Age of onset, optimal age of intervention
- Strength of environmental component and other non-genetic risk contributors
- Genetic architecture
- Burden/invasiveness of intervention
- Implementation model
- Availability of hard endpoints



GM XIII: Genomics and Public Health
June 2-3, 2020, Rockville MD

- Review and highlight landscape of genomic medicine being applied to population and public health in U.S. and public health models that may be informative
- Explore significant barriers in reaching underserved communities and put them on equal footing with those who have access to academic health centers
- Define a research agenda building upon these efforts that will enable implementation of genomic medicine into settings not previously addressed by NHGRI

NHGRI's Genomic Medicine Research Program, 2/4/20

Program	Goal	Σ$M	Years
UDN[1]	Diagnose rare and new diseases by expanding NIH's Undiagnosed Diseases Program	237	FY13-22
NSIGHT[2]	Explore possible uses of genomic sequence information in the newborn period	26	FY13-18
CSER[3]	Generate evidence of clinical utility of sequencing in diverse clinical settings	166	FY12-20
eMERGE[4]	Use biorepositories with EMRs for genomics; assess generalizability and clinical impact of genomic risk prediction	206	FY07-24
IGNITE[3]	Conduct pragmatic clinical trials of genomic interventions (*APOL1* testing and PGx for pain and depression treatment)	76	FY13-22
ClinGen[4]	Develop and disseminate consensus information on genes and variants relevant to clinical care	73	FY13-20
Investigator-Initiated	Clinical sequencing research, HIV/AIDS drug response and co-morbidities, serious ADRs, pharmacogenomics, etc.	41	FY15-22
Training	Institutional training grants, fellowships, career development	15	FY16-21

[1]NIH Common Fund; [2]Co-Funded by NICHD; [3]Co-Funded by NCI; [4]Co-Funded by OD.