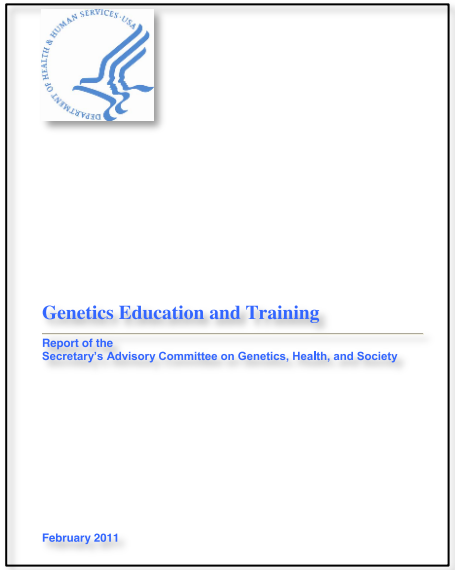
Global Genomic Medicine Collaborative: Genomics Education

Bruce R. Korf, MD, PhD
Department of Genetics
University of Alabama at Birmingham

Evidence from the United States and abroad suggests inadequate genetics education of health care professionals as a significant factor limiting the integration of genetics into clinical care. Specific inadequacies include the amount and type of genetics content included in undergraduate professional school curricula and the small amount of genetics-related knowledge and skills of physicians, nurses, and other health professionals once they enter clinical practice. Modifications in medical, dental, nursing, public health, and pharmacy school curricula and in medical residency training programs are needed to ensure that health care professionals entering the workforce are well-trained in genetics.



Case 1

- 65 year old woman referred to UAB Undiagnosed Diseases Program
- Obesity, chronic fatigue, heat intolerance
- Interested in whole genome sequencing
- Incidental diagnosis of spinocerebellar ataxia 14
- Exam revealed no neurological signs
- No family history of spinocerebellar ataxia

Interpretation

This individual possesses DNA sequence variants of unknown clinical significance in one of the sequenced genes. In addition they possess additional variants of unknown significance or borderline repeat expansion mutations in another gene. It cannot be determined whether this individual is likely to be affected with, or predisposed to developing ataxia associated with the specific borderline repeat(s) or DNA sequence variants of unknown significance. Therefore the interpretation is indeterminate. Please refer to the Comments section for further information and please contact our genetic counselor at 1-800-394-4493 to discuss these results.

Technical Results

Test	Results	Alert	Repeats
SCA1	Normal		32 and 30
SCA2	Normal		22 and 22
SCA3	Normal		28 and 14
SCA6	Normal		13 and 12
SCA7	Normal		10 and 10
SCA8	Normal		24 and 24
SCA10	Normal		16 and 12
SCA17	Normal		39 and 38
DRPLA	Normal		19 and 18
FRDA1	Normal		4 and 4

APTX Result: Normal

SCA14 Result: Variants of **Unknown significance**
SETX Result: Variants of **Unknown significance**
POLG1 Result: Normal
SCA5 Result: Normal
SIL1 Result: Normal
TTPA Result: Normal
KCNC3 Result: Normal

SCA14 Variant 1: Transition T > C
Nucleotide position: 1497
Codon position: 499
Amino acid change: None
DNA variant type: Variant of unknown significance

SETX Variant 1: Transition G > A
Nucleotide position: IVS13+10
Codon position: DNR
Amino acid change: DNR
DNA variant type: Variant of unknown significance, heterozygous

SETX Variant 2: Transition G > A
Nucleotide position: 6507
Codon position: 2169
Amino acid change: None
DNA variant type: Variant of unknown significance, heterozygous

Outcome

- VUS reclassified as benign variant (7 years later)
- WGS done and no pathogenic variants found to explain her phenotype

Case 2

- 32 year old man seen for genetic counseling
- Family history of breast cancer in his father and paternal aunt
- Paternal aunt positive for pathogenic BRCA2 variant
- Has two siblings without cancer, both also positive
- He was tested and was told result was negative – presented for options for additional testing

Collection DT	Specimen	Test Name	Result	Units
11/24/2015 10:50	BLOOD	BRCA1 SEQUENCING	NEGATIVE	
"	"	INTERP SUMM	SEE NOTE	
"	"	BRCA1 SEQ INTERP	SEE NOTE	
"	"	BRCA1 DEL/DUP	NEGATIVE	
"	"	BRCA1 DEL/DUP INT	SEE NOTE	
"	"	BRCA2 SEQUENCING	SEE NOTE	
"	"	BRCA2 SEQ INTERP	SEE NOTE	
"	"	BRCA2 DEL/DUP	NEGATIVE	
"	"	BRCA2 DEL/DUP INT	SEE NOTE	
"	"	COMP INTERP	SEE NOTE	
"	"	ADDITIONAL INFO	SEE NOTE	

Comment: Interpretation Summary
Comment: POSITIVE FOR A KNOWN PATHOGENIC MUTATION
Comment: BRCA1 Seq Interp
Comment: NO MUTATION DETECTED
Comment: BRCA1 Del/Dup Interp
Comment: NO MUTATION DETECTED
Comment: BRCA2 Sequencing
Comment: c.1755_1759del (p.Lys585Asnfs*3)
Comment: BRCA2 Seq Interp
Comment: KNOWN PATHOGENIC
Comment: BRCA2 Del/Dup Interp
Comment: NO MUTATION DETECTED
Comment: Comprehensive Interp
Comment: This test has identified one copy of the
Comment: c.1755_1759del mutation (also known as
Comment: c.1755_1759delGAAAA) in exon 10 of the BRCA2 gene.
Comment: This frameshift mutation causes the premature
Comment: termination of BRCA2 protein synthesis
Comment: (p.Lys585Asnfs*3), and is described in multiple
Comment: BRCA online databases as being pathogenic (see the
Comment: Breast Cancer Information Core
Comment: https://research.nhgri.nih.gov/projects/bic/,
Comment: ClinVar http://www.ncbi.nlm.nih.gov/clinvar/, and
Comment: ARUP for BRCA2
Comment: http://arup.utah.edu/database/BRCA/Variants/BRCA2)
Comment: . Therefore, this individual is at increased risk

(continued)

Comment: of developing BRCA related cancers. Genetic
Comment: counseling and DNA testing for at-risk family
Comment: members are recommended. Laboratory results and

Competencies

- Recognize indications for testing
- Select appropriate family member to test first
- Discuss issues of payment/risks/benefits
- Select a laboratory
- Interpret report – recognize limitations
- Genomic sequencing – recognize potential for secondary findings
- Refer to specialist as needed
- Discuss results with family

SPECIAL ARTICLE | Genetics inMedicine

Framework for development of physician competencies in genomic medicine: report of the Competencies Working Group of the Inter-Society Coordinating Committee for Physician Education in Genomics

Bruce R. Korf, MD, PhD[1], Anna B. Berry, MD[2,3], Melvin Limson, PhD[4], Ali J. Marian, MD[5], Michael F. Murray, MD[6], P. Pearl O'Rourke, MD[7], Eugene R. Passamani, MD[8], Mary V. Relling, PharmD[9], John Tooker, MD, MBA[10], Gregory J. Tsongalis, PhD[11,12] and Laura L. Rodriguez, PhD[8]

Completion of the Human Genome Project, in conjunction with dramatic reductions in the cost of DNA sequencing and advances in translational research, is gradually ushering genomic discoveries and technologies into the practice of medicine. The rapid pace of these advances is opening up a gap between the knowledge available about the clinical relevance of genomic information and the ability of clinicians to include such information in their medical practices. This educational gap threatens to be rate limiting to the clinical adoption of genomics in medicine. Solutions will require not only a better understanding of the clinical implications of genetic discoveries but also training in genomics at all levels of professional development, including for individuals in formal training and others who long ago completed such training. The National Human Genome Research Institute has convened the Inter-Society Coordinating Committee for Physician Education in Genomics (ISCC) to develop and share best practices in the use of genomics in medicine. The ISCC has developed a framework for development of genomics practice competencies that may serve as a starting point for formulation of competencies for physicians in various medical disciplines.

Genet Med advance online publication 24 April 2014

Key Words: competencies; education; genomic medicine; genomics

The promise of genomics to maintain health, facilitate diagnosis, and cure or mitigate disease is dependent on the skillful translation of genomic science into meaningful action at the bedside and in the clinic.[1,2] Surveys of both primary-care and specialist physicians, often by their professional societies, reveal unease, and even unwillingness, to use genomic data.[3,4] The use of genomics in caring for patients with certain cancers and for some pediatric patients is increasing in routine diagnosis and treatment, and this trend is likely to expand to other areas of medical practice in the coming years.[5,6]

Nearly half of practicing clinicians in the United States are more than 50 years of age; medical school and residency training for these physicians occurred before the completion of the Human Genome Project and the breakthrough advances in genomic medicine.[7] Current trainees are faced with a rate of progress in genomics that renders much of what they have learned out of date by the time they enter practice. Considering this rapid rate of change, substantial reductions in the cost of genome sequencing, and the increasing relevance of genomic information to the practice of medicine, the barriers to implementing genomic discoveries within medical practice have to be overcome. Moreover, misuse of genomics by untrained health-care providers may incur cost without advantage and may result in harm to patients based on inaccurate diagnosis or use of unnecessary or incorrect tests.

The National Human Genome Research Institute, together with 23 professional societies, 15 other institutes at the National Institutes of Health, and other organizations interested in physician education, developed the Inter-Society Coordinating Committee for Physician Education in Genomics (ISCC) in the spring of 2013 (see **Supplementary Data S1** online). ISCC member organizations focus on physician training, starting with medical school matriculation and continuing through residency and fellowship, for active clinicians.[8] The ISCC seeks to "improve genomic literacy of physicians and other practitioners and to enhance the practice of genomic medicine through sharing of educational approaches and joint identification of educational needs." The ISCC developed four working groups: Genomic Medicine Competencies, Educational Products, Use Cases, and Specialty Boards (see **Supplementary Data S1** online).

The Genomic Medicine Competencies Working Group was charged with the development of a framework whereby

[1]Department of Genetics, University of Alabama at Birmingham, Birmingham, Alabama, USA; [2]CellNetix Pathology & Laboratories, Swedish Cancer Institute, Seattle, Washington, USA; [3]Department of Pathology, University of California, San Francisco, San Francisco, California, USA; [4]Association for Molecular Pathology, Bethesda, Maryland, USA; [5]Center for Cardiovascular Genetics, University of Texas Health Sciences Center, Houston, Texas, USA; [6]Genomic Medicine Institute, Geisinger Health System, Danville, Pennsylvania, USA; [7]Partners HealthCare System, Boston, Massachusetts, USA; [8]National Human Genome Research Institute, Bethesda, Maryland, USA; [9]Department of Pharmaceutical Sciences, St Jude Children's Research Hospital, Memphis, Tennessee, USA; [10]American College of Physicians, Philadelphia, Pennsylvania, USA; [11]American Association for Clinical Chemistry, Washington, DC, USA; [12]Department of Pathology, Geisel School of Medicine at Dartmouth, Dartmouth Hitchcock Medical Center and Norris Cotton Cancer Center, Lebanon, New Hampshire, USA. Correspondence: Bruce R. Korf (bkorf@uab.edu)

Submitted 20 February 2014; accepted 12 March 2014; advance online publication 24 April 2014. doi:10.1038/gim.2014.35

ISCC Compete icine

- Elicit, document, an tinent to patient's clinical stat
- Utilize genomic testi nanagement
- Utilize genomic infor ons
- Support the use of g iagnosis and management of can omatic genetic changes
- Utilize genomic test s to human health and disease, therapy of infectious diseases

Genomic Testing

EPA: Utilize genomic testing appropriately to guide patient management

Patient Care

- Discuss the indications for genomic testing – specifically the benefits, risks, and alternatives
- Explain the implications of placing genomic test results in the patient's medical record
- Discuss the possibility of incidental findings and how they will be handled
- Discuss risks of having genomic testing done: *e.g.*, psychological to the individual as well as family; the potential for discrimination; potential effect on insurance coverage, *etc.*
- Explain to a patient issues of costs and financial coverage of genomic testing
- Order, interpret, and communicate the results of appropriate genomic tests, within the physician's scope of practice
- Provide referral to an appropriate specialist for genomic testing of a condition outside the physician's scope of practice
- Respond to the results of an abnormal genetic screening test, such as newborn screening, including immediate management and appropriate referral

Knowledge for Practice

- Describe the major forms of genomic variability
- Explain how different genomic changes may result in different phenotypes
- Recognize that genomic tests require interpretation with respect to the patient's clinical status (*e.g.*, pathogenic, likely pathogenic, benign, *etc.*)
- Explain the concepts of analytic validity, clinical validity, clinical utility as they relate to genomic testing
- Recognize that medically "non-actionable" genomic results can be useful to the patient and family (*i.e.*, personal utility)

Practice-Based Learning and Improvement

- Incorporate genomic findings into the health record and patient care plan
- Have a method for periodic review of 'new' genomic interpretation for clinical applications.

Interpersonal and Communication Skills

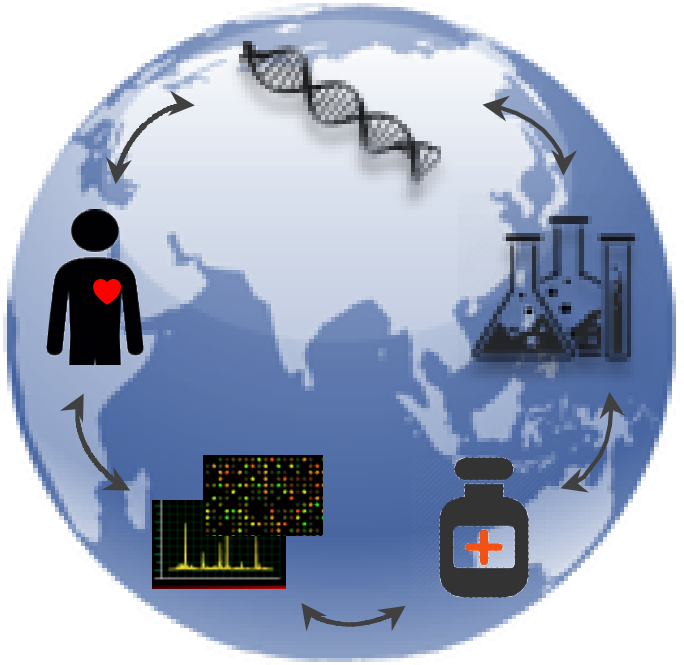
- Ensure that undergoing genomic testing is a joint decision of the patient and the physician
- Explain and document findings from genomic testing to patient, including implications for other family members
- Facilitate access to resources to enhance patient learning about the results of genomic testing
- Address the needs of the patient as an individual as well as the needs of family members

Global Genomic Medicine Collaborative (G2MC)

- Genomic medicine is global
- Genome ‘hubs’ in most continents
- Explore synergies, redundancies, collaborative opportunities
- Opportunities to advance the genome sciences as a global agenda and to impact global health

2nd Global Genomic Medicine Collaborative Meeting

6 – 7 November 2015, Singapore



Implementing Genomic Medicine into Practice

Infographics | Media Room | Videos | NAM Perspectives

The National Academies of SCIENCES · ENGINEERING · MEDICINE

HEALTH AND MEDICINE DIVISION

ABOUT HMD | PUBLICATIONS | ACTIVITIES | MEETINGS | Explore by Topic | Keyword Search

Share | Tweet | G+1 | Share | share | Email | Print

ACTION COLLABORATIVES

Global Genomic Medicine Collaborative (G2MC)

Global Genomic Medicine Collaborative

The Global Genomic Medicine Collaborative (G2MC) is an action collaborative among global leaders in the implementation of genomic medicine in clinical care. Arising from the 2014 Global Leaders in Genomic Medicine Summit, the purpose of G2MC is to identify opportunities and foster global collaborations for enabling the demonstration of value and the effective use of genomics in medicine. Engaging multiple stakeholders across the globe, the G2MC group, under the auspices of the Roundtable on Genomics and Precision Health, seeks to improve global health by catalyzing the implementation of genomic tools and knowledge into health care delivery globally. To accomplish these goals, seven working groups were created, including communications, education, evidence, IT/bioinformatics, pharmacogenomics, policy, and a steering group to guide and support efforts among working groups.

Specifically, it is intended to:

- Serve as nexus, clearinghouse, and knowledge base for genomic medicine activities globally;
- Develop opportunities for global genomic medicine demonstration projects (implementation and outcomes research) and;
- Capture and disseminate best practices for genomic medicine (in bioinformatics, education, evidence, pharmacogenomics, policy) across the global genomic medicine community.

Current Activities

The purpose and goals of the Global Genomic Medicine Collaborative (G2MC):

- Develop projects with global participation
  - Opportunities to disseminate learnings for genomic medicine implementation
  - Educational platforms to support genomic medicine projects
  - Community engagement and access to global genomic medicine expertise
- Creation of a registry or catalog of genomic medicine projects and programs across the globe to stimulate collaboration and efficiency in translation
- Be a global policy forum for genomic medicine
  - Mapping the global genomic medicine landscape particularly as it relates to policy and implementation
- Global eradication of preventable Stevens Johnson Syndrome/Toxic Epidermal Necrolysis

Previous Meetings:

November 6-7, 2015 - Implementing Genomic Medicine into Practice

The meeting objectives were to:

- Highlight nations or organizations around the world that are implementing genomic medicine into practice
- Foster/facilitate collaborations to enable the implementation of genomic medicine
- Highlight best practices and lessons learned to enable others to effectively implement genomic medicine approaches
- Identify and develop solutions for overcoming obstacles to genomic medicine implementation
- Identify and discuss regulations and policies that impact the implementation of genomic medicine
- Create a global tool box for implementation of genomic medicine into practice

Agenda

Attendee List

G2MC Group Photo

January 8-9, 2014 - Global Leaders in Genomic Medicine

The goals of the meeting were to:

- Identify areas of active translational and implementation research, potential common strategies, and opportunities for collaborative efforts.
- Identify common barriers to implementation of genomics in healthcare and a policy agenda relevant to advances in the field.
- Identify nations with unique capabilities (such as national healthcare systems) that may allow rapid implementation and measures of key outcomes.
- Discuss opportunities (such as national healthcare system) that may allow rapid implementation and measures of key outcomes.

Participants (View Bios)

Back to Activity

Action Collaboratives

- DIGITizE: Displaying and Integrating Genetic Information Through the EHR
- Genomics and Population Health - A Precision and Public Health Activity

Stay up to date!

Sign up to receive e-mail updates about HMD's work.

Sign Up Now

Roundtable Members

- Geoffrey Ginsburg, Co-Chair
- Sharon Terry, Co-Chair

View Full Roundtable Roster

Activity Staff

- Sarah Beachy, Activity Director

View Full Activity Staff Roster

Activity Contact Information

For More Information Contact

Board on Health Sciences Policy

Phone: 202-334-2914
Fax: 202-334-1329
E-mail: Genomics@nas.edu

Mailing Address

Keck Center
500 Fifth St. NW
Washington, DC 20001

Last Updated: 4/15/2016, 9:24 AM | Copyright © 2016 National Academy of Sciences. All Rights Reserved.
Contact Us: Phone (202) 334-2352 Email: HMD-NASEM@nas.edu | Privacy Policy

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]*

Around the world, innovative genomic-medicine programs capitalize on singular capabilities arising from local health care systems, cultural or political milieus, and unusual selected risk alleles or disease burdens. Such individual efforts might benefit from the sharing of approaches and lessons learned in other locales. The U.S. National Human Genome Research Institute and the National Academy of Medicine recently brought together 25 of these groups to compare projects, to examine the current state of implementation and desired near-term capabilities, and to identify opportunities for collaboration that promote the responsible practice of genomic medicine. Efforts to coalesce these groups around concrete but compelling signature projects should accelerate the responsible implementation of genomic medicine in efforts to improve clinical care worldwide.

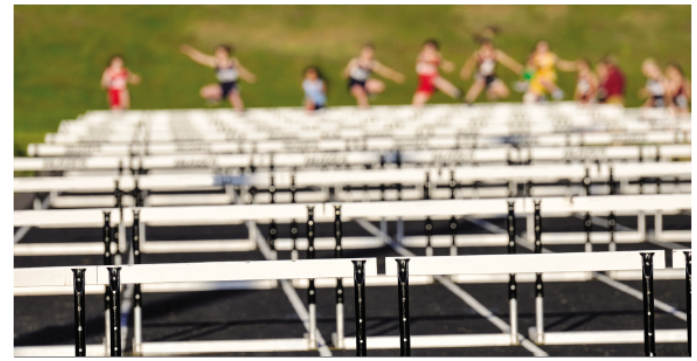
The growing number of advances in human genomic research that are directly relevant to disease diagnosis, treatment, and prevention coupled with the declining cost of genome sequencing has promoted the use of genomic technologies in routine clinical care (*1*). Among the many challenges to widespread implementation of genomic medicine, what looms largest is the lack of evidence to demonstrate improved clinical or economic outcomes (*2*). Other needs include standardization and quality assurance of genomic data produced by clinical laboratories, a clinical-informatics infrastructure for managing genomic information, education for health professionals and patients in using the information, and policies for data sharing that permit ongoing capture of generalizable clinical experiences in what has been termed "evidence-generating medicine" (*3*). A host of ongoing efforts exist worldwide to establish national implementation strategies for genomic medicine (table S1) (*4*), but many such efforts are being conducted in relative isolation. Sharing of strategies, data, and standards could minimize wasteful duplication and speed progress in identifying genomics-based interventions and translating them to the clinic.

To assess the current global state of the art (*2*), the U.S. National Human Genome Research Institute and the U.S. National Academy of Medicine convened 90 leaders in genomic medicine from the United States and 25 other countries on five continents for a Global Leaders in Genomic Medicine symposium in 2014 (table S1). Although the organizers attempted to identify and invite every nation working on the implementation of genomic medicine, participation was somewhat restricted by the lack of systematic information on such efforts and limited travel funding [see full list of participating countries at www.genome.gov/27555775]. Here we summarize efforts described by the participants, with an emphasis on (i) regions with singular capabilities because of the structures of their health care systems, cultural or political readiness for implementation, or unusual disease burdens or risk-allele frequencies; (ii) the current state of implementation in the various countries and capabilities desired over the next 3 to 5 years; and (iii) opportunities for collaboration to promote the responsible implementation of genomic medicine.

INTERNATIONAL LANDSCAPE

Early efforts at genomic-medicine collaborations include the European Association for Predictive, Preventive, and Personalised Medicine (EPMA), the European Commission's EuroBioForum and observatory, and the Genomic Medicine Alliance (table S1) (*5*), which have spearheaded promising projects such as the application of genome sequencing in pharmacogenomics and the development of online pharmacogenomic resources. Related efforts include the International Rare Disease Research Consortium (IRDiRC), which is developing new diagnostic strategies and therapies for rare diseases; the Global Alliance for Genomics and Health (GA4GH), which promotes responsible sharing of genomic data for research (*6*); and EuroGentest (table S1), which is drafting professional guidelines for diagnostic DNA sequencing.

In an informal poll of participants prior



CREDIT: PUHERRERA/ISTOCKPHOTO

Teamwork: Clearing of hurdles to the clinical translation of genomic medicine demands a unified focus.

2015: Global Attendance

Working Groups

- IT/bioinformatics
- Education/workforce
- Pharmacogenomics
- Evidence
- Policy
- Sequencing

Education
[Bruce Korf, Vajira Dissanayake]

- Genomic Medicine Workforce
  - What are the kinds of health professionals who practice genomic medicine in your country?
  - What is the training required for these professionals?
  - What is their scope of practice?
  - How do other health professionals interact with genomic medicine professionals, if they exist?
  - Are genomic medicine training programs in consideration if they do not currently exist?
- Method
  - Develop survey to share with members and other international contacts
  - Report and store information on central web site

Education, continued

- Case Based Teaching
  - Develop examples of cases used for teaching genomic medicine
  - Place in open-source format for use by G2MC members to use or modify
  - Expect that those who modify a case will post the modification
  - Attention to use of copyrighted material or patient photos
- Grand Rounds
  - WebEx webinars hosted by different members of G2MC
    - Monthly meetings
    - Some participate in real time, others by viewing recording
  - Content
    - Country-specific projects
    - Case conferences
  - Q&A
    - Real time for those who can participate
    - Maintain online videos and discussions

Global Genomic
Medicine Collaborative

webex

Grand Rounds

03 August 2016 - PDT 06.00 am; CDT 08.00 am; EDT 09.00 am; London 2.00 pm; Dubai 05.00 pm; New Delhi 06.30 pm; Manila 09.00 pm; Brisbane 11.00 pm

Regeneron / Geisinger DiscovEHR Programme

David Carey, PhD
Director
Weis Center for Research
Geisinger Health System
USA

Visit **bit.ly/g2mcaugust** to register

Supported by:

Home
Trending

BEST OF YOUTUBE
Music
Sports
Gaming
Movies
TV Shows
News
Live
Spotlight
360° Video

Browse channels

Sign in now to see your channels and recommendations!

Sign in

YouTube Red

Global Genomic Medicine Collaborative Grand Rounds

Subscribe 12

Uploads

G2MC Grand Rounds - Session 03
32 views • 4 weeks ago

G2MC Grand Rounds - Session 02
17 views • 1 month ago

G2MC Grand Rounds - Session 01
49 views • 2 months ago

Created playlists

G2MC Grand Rounds

G2MC Grand Rounds - Session 01	50:38
G2MC Grand Rounds - Session 02	1:03:45
G2MC Grand Rounds - Session 03	54:26

View full playlist (3 videos)

G2MC Grand Rounds

May: UAB Undiagnosed diseases programme – Dr. Bruce Korf

June: Pharmacogenomic Initatives in Thailand – Dr. Wasun Chantratita, Mahidol University, Thailand

July: The BEST Network as a online tool for sharing and delivery of online genetic resources in genetics – Nicholas Hawkins, University of Queensland, Australia

August: Regeneron/Geisinger: DiscovEHR Programme – David Cary PhD, Geisinger Health System

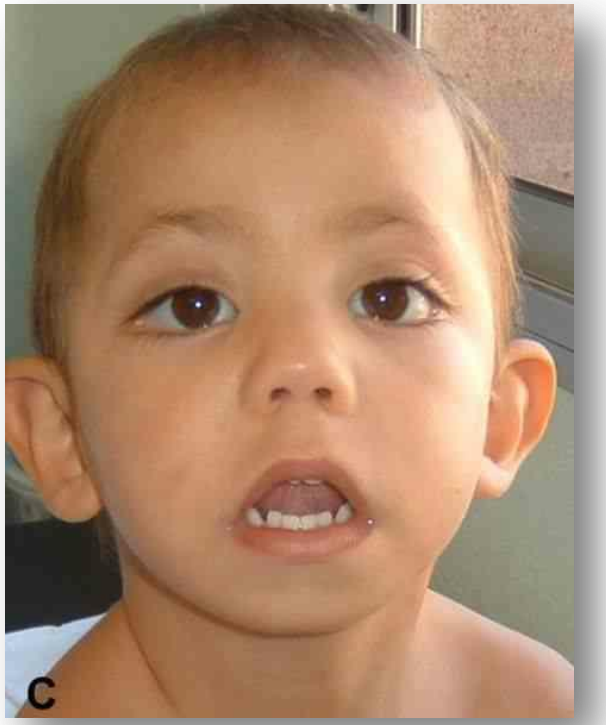
YouTube Chanel Link
https://www.youtube.com/channel/UCOMoopNfFVht04ukMMmHXKg

To subscribe to the email list for notifications

Please send a blank email to subscribe-g2mc@hgucolombo.org

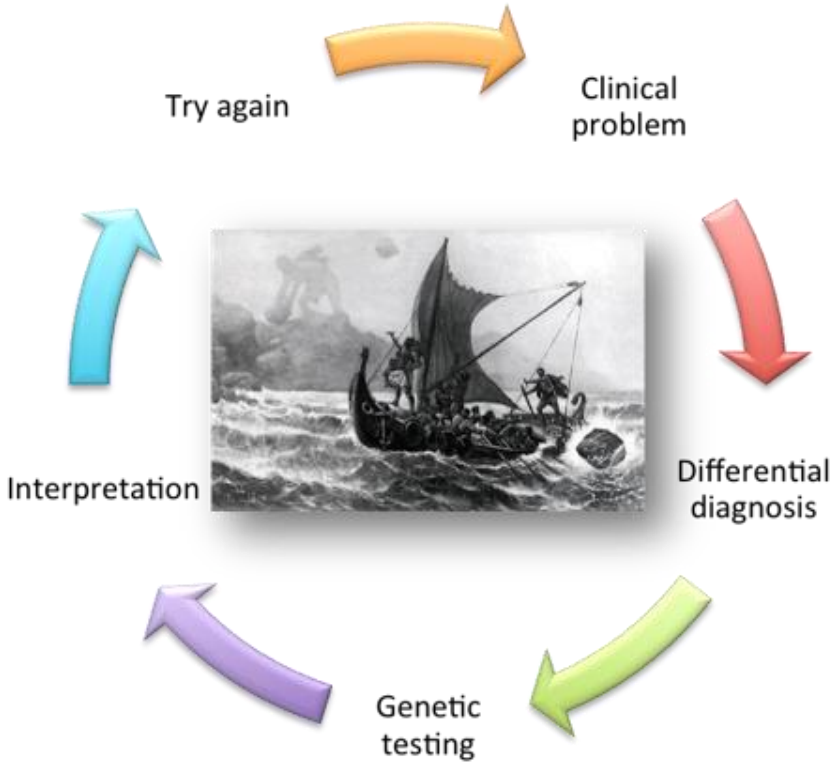
Case 4.1

Alex is a four-year old boy with developmental delays and dysmorphic features. He has a small VSD and short stature. He is an only child and referral for genetics evaluation has not revealed a diagnosis.



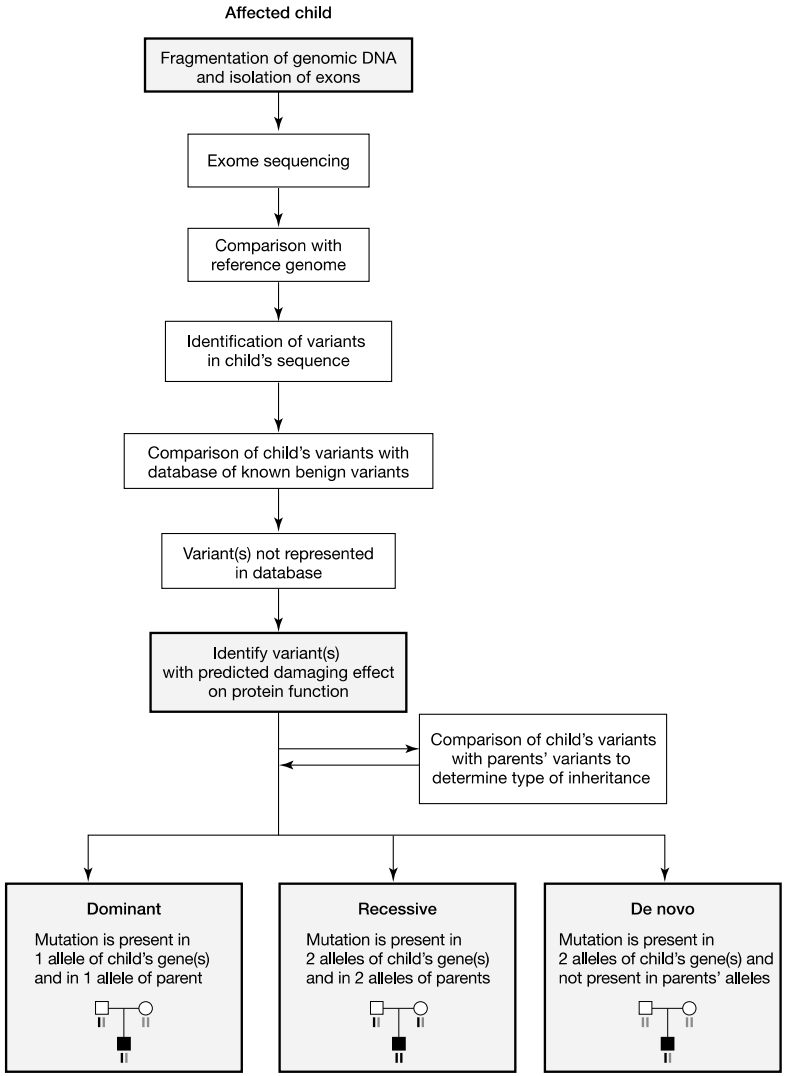
Cuscó I, del Campo M, Vilardell M, González E, Gener B, Galán E, Toledo L, Pérez-Jurado LA. Array-CGH in patients with Kabuki-like phenotype: identification of two patients with complex rearrangements including 2q37 deletions and no other recurrent aberration. BMC Med Genet. 9, 27. 2008. doi:10.1186/1471-2350-9-27. PMID 18405349.

The Diagnostic Odyssey



Case 4.2

He is seen by a geneticist, who recommends exome sequencing. This is done, and he is found to have a mutation in the *MLL2* gene, indicative of Kabuki syndrome.



JAMA. 2013;309(14):1511-1521

Case 4.3

When Alex's parents speak with the geneticist they learn something else unexpected: Alex carries a known pathogenic mutation in the *BRCA1* gene. There is no known family history of breast or ovarian cancer, but Alex's father was adopted.

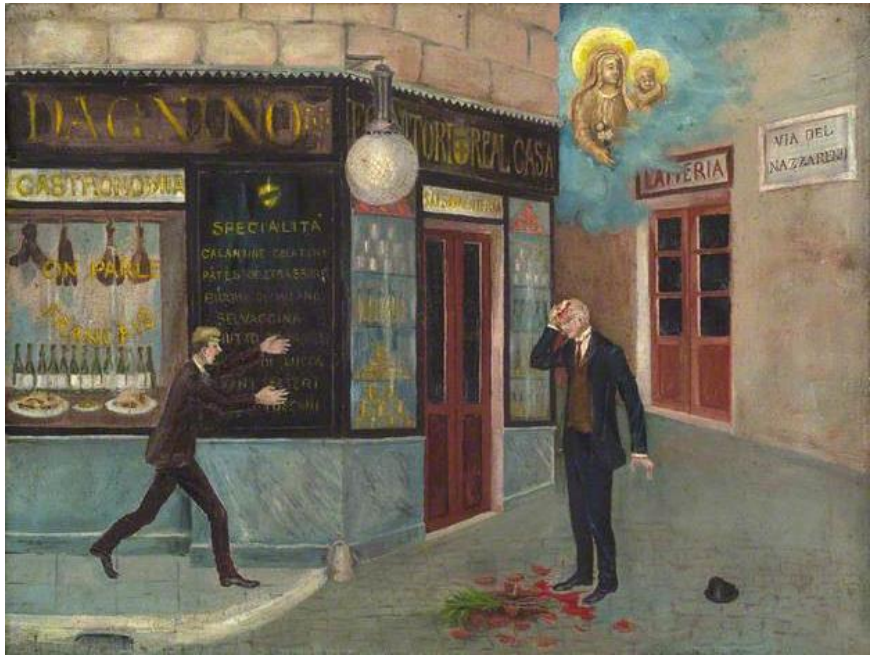


photo credit: Wellcome Library

Incidental Findings

American College of Medical Genetics and Genomics

ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing

Robert C. Green, MD, MPH[1,2], Jonathan S. Berg, MD, PhD[3], Wayne W. Grody, MD, PhD[4-6], Sarah S. Kalia, ScM, CGC[1], Bruce R. Korf, MD, PhD[7], Christa L. Martin, PhD, FACMG[8], Amy McGuire, JD, PhD[9], Robert L. Nussbaum, MD[10], Julianne M. O'Daniel, MS, CGC[11], Kelly E. Ormond, MS, CGC[12], Heidi L. Rehm, PhD, FACMG[2,13], Michael S. Watson, MS, PhD, FACMG[14], Marc S. Williams, MD, FACMG[15], Leslie G. Biesecker, MD[16]

Genet Med. 2013 Jul;15(7):565-74. doi: 10.1038/gim.2013.73. Epub 2013 Jun 20.

Recommendations

- Constitutional mutations on minimal list should be reported regardless of age of patient
- Laboratories should seek and report specific types of mutations on list
- Ordering clinician responsible for pre- and post-test counseling
- Patients may opt out of learning about incidental findings

Gene List

Type	Genes
Tumor Predisposition (Breast/ovarian, Li-Fraumeni, Peutz-Jeghers, Lynch, FAP, Polyposis, Von Hippel-Lindau, MEN1/2, Medullary thyroid ca, PTEN hamartoma, retinoblastoma, Paraganglioma/Pheo, TSC, WT1-related Wilms', NF2)	*BRCA1, BRCA2, TP53, STK11, MLH1, MSH2, MSH6, PMS2, APC, MUTYH, VHL, MEN1, RET, NTRK1, PTEN, RB1, SDHD, SDHAF2, SDHC, SDHB, TSC1, TSC2, WT1, NF2*
Connective Tissue Dysplasia (EDS vascular type, Marfan, Loeys-Dietz, Familial thoracic and aortic aneurysms/dissections	*COL3A1, FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYLK, MYH11*
Cardiomyopathy (Hypertropic, dilated)	*MYBPC3, MYH7, TNNT2, TNNI3, TPMN1, MYL3, ACTC1, PRKAG2, GLA, MYL2, LMNA*
Arrhythmia (Arrhythmogenic RVCM, Romano-Ward, Brugada)	*RYR2, PKP2, DSP, DSC2, TMEM43, DSG2, KCNQ1, DCNH2, SCN5A*
Hypercholesterolemia	*LDLR, APOB, PCSK9*
Malignant hyperthermia	*RYR1, CACNA1S*

Revolutionising Biomedical Education

BEST - the Biomedical Education Skills and Training Network is a digitally-powered community of experts who share a vision: that every student and teacher will have access to the best biomedical education.

WATCH THE VIDEO

DISCIPLINARY LOOPS

The value of the network is its community: experts like you, sharing their courseware, medical images and expertise to build the future of biomedicine.

EXPLORE LOOPS

COURSEWARE CATALOGUE

BEST couseware is rich, interactive and adaptive, and powered by real-time learning analytics. Teach lessons as is, or adapt it to suit your needs.

BROWSE THE CATALOGUE

SLICE

Search, annotate and collaborate on premium medical images with the world's most advanced cloud-based biomedical image bank.

DISCOVER SLICE

JOIN NOW WHY JOIN? >

MENDELIAN INHERITANCE

Resource Visibility: Public

Subscribe

Chapter 1: Basic Patterns of Mendelian Inheritance

Description Related

AUTHOR

Bruce Korf MD, PhD

DESCRIPTION

Learn about the patterns of single gene inheritance.

Last reviewed: March 08, 2016.

Topics: Genetics

Licensing Information: All Rights Reserved

Transcript Comments

Mendelian Inheritance by Dr. Bruce Korf, in collaboration with the University of Alabama at Birmingham.

My name is Bruce Korf.

I'm a Medical Geneticist in the Department of Genetics at University of Alabama at Birmingham.

This talk will focus on the principles of Mendelian inheritance.

We'll first describe the basic patterns of Mendelian inheritance, that is autosomal recessive, autosomal dominant, and sex-linked.

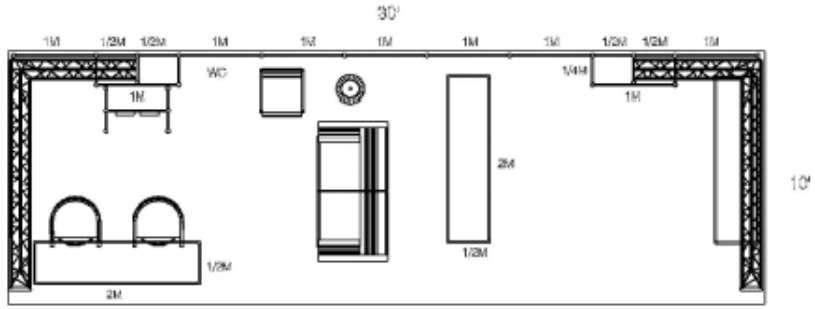
We'll explain the concepts of penetrance and

Call +1 617.919.4556

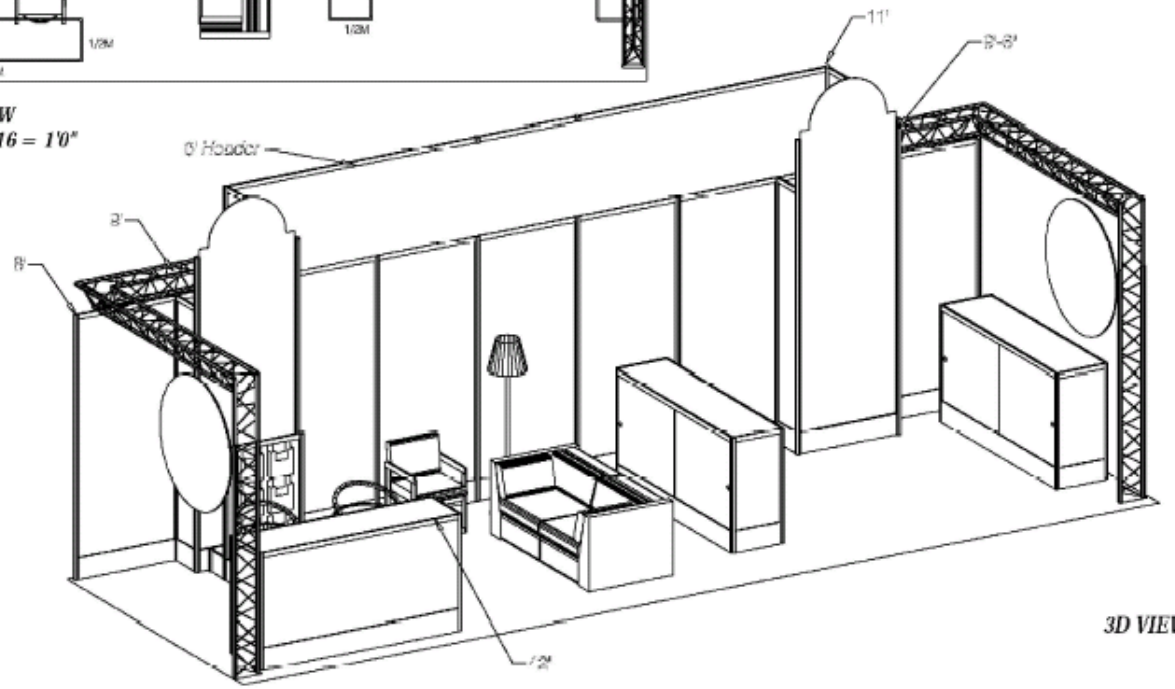
Contact Us Via Email or Via Our Contact Form

OPENPediatrics
Boston Children's Hospital
Landmark Center, 7th Floor
401 Park Drive
Boston, MA 02215

- Swipe badge in computer
- Assignment to
  - Hemochromatosis
  - Breast cancer
  - MEN 2
- Make counseling appointment



PLAN VIEW
SCALE: 3/16 = 1'0"

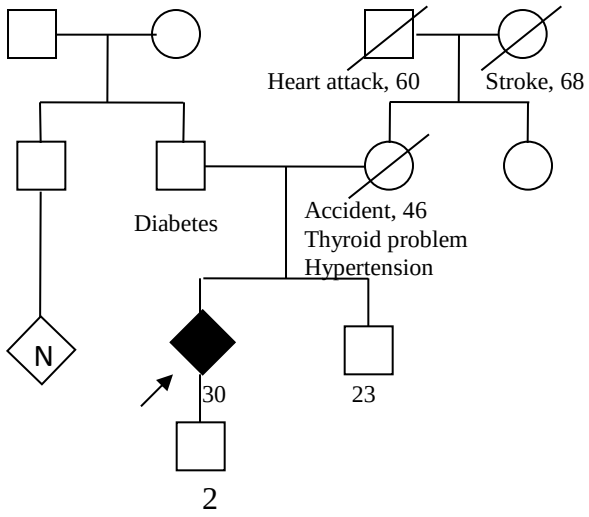


3D VIEW

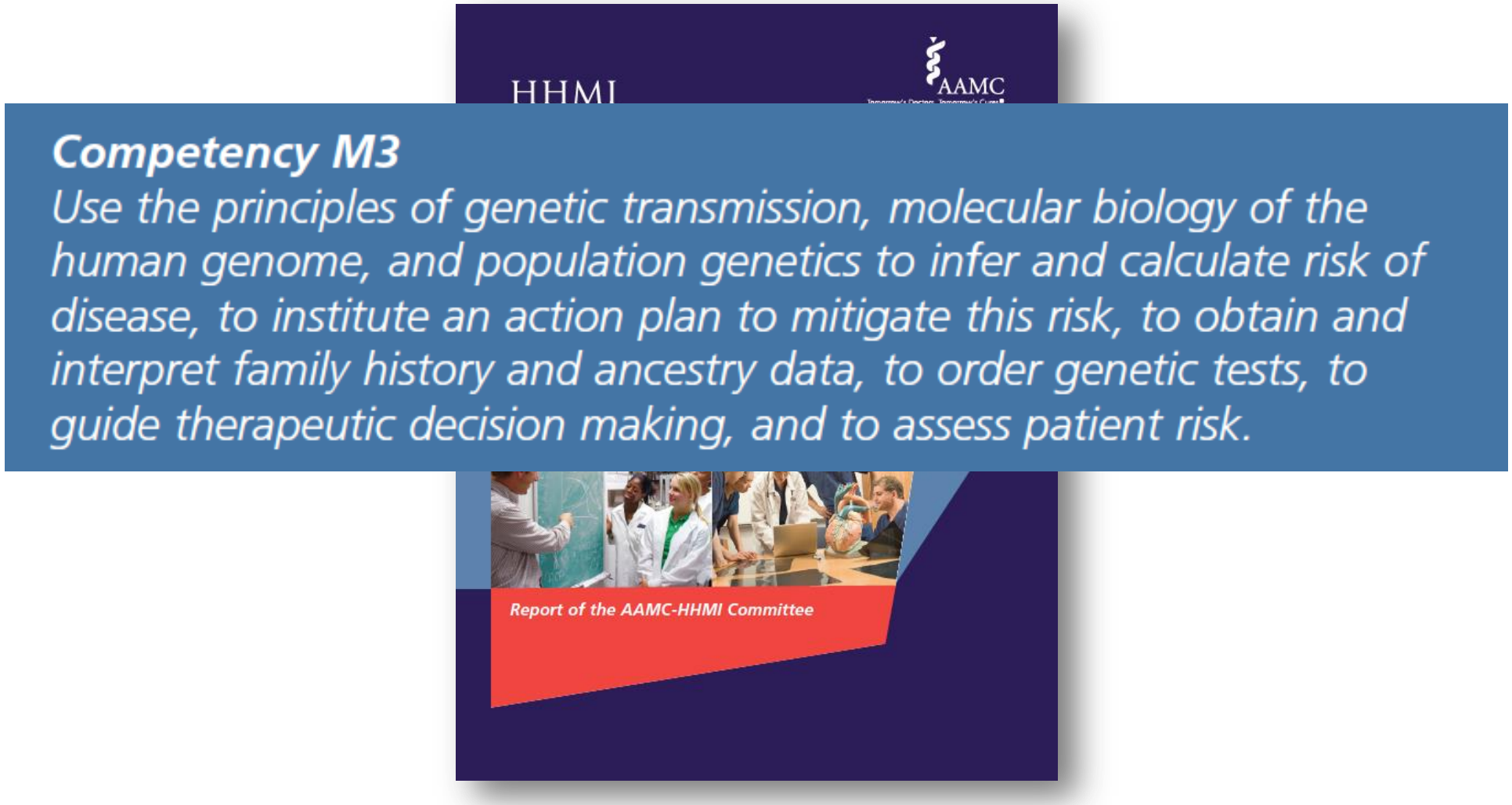
MEN2 Case

You are 30 years old and have been recently diagnosed with medullary thyroid carcinoma. Your medical history is otherwise unremarkable. Your endocrinologist tells you he would like to refer you to a genetic counselor because this particular type of thyroid cancer can run in families. You meet with a genetic counselor who gathers family history information.

The only potentially significant finding is some thyroid problem your mother had as a child, but records are not available. You have a healthy 2-year-old son and a 23-year-old brother. A geneticist does a physical exam, which she says is unremarkable. After a lengthy discussion, you decide to pursue testing of the *RET* gene and have your blood drawn. You arrange to return in four weeks to get the test results.



Medical Education



ACMGF Summer Scholars Program

EDUCATION

How to know when physicians are ready for genomic medicine

Jason L. Vassy,[1,2,3*] Bruce R. Korf,[4] Robert C. Green[3,5]

Despite perceptions to the contrary, physicians are as prepared for genomic medicine as they are for other medical innovations; educational initiatives and support from genetics specialists can enhance clinical practice.

With the tremendous investment in the genomic sciences over the last two decades, the biomedical community is eager to apply new genomic knowledge to patient care. Genomic testing, including whole-genome and exome sequencing, has demonstrated clinical utility in certain contexts (*1*). However, the workforce of fewer than 2000 board-certified medical geneticists is insufficient to meet the demand created by the greater prominence of genomics in clinical medicine (*2*). As a result, physicians without specialized genetics training will be increasingly called upon to order genomic testing and use the results in the care of their patients. At the same time, several studies have found that physicians report "unpreparedness" and low confidence in their ability to apply genomic data to patient care (*3*). Here we discuss how to assess whether physicians are ready for the genomic revolution and whether previous medical innovations have been held to the same standards.

POTENTIAL PERILS OF UNPREPAREDNESS

Despite recent standardization efforts, most molecular laboratories do not currently use a uniform approach to the clinical interpretation of the large number of genetic variants revealed by genome sequencing, most of which have unknown clinical significance. Even for variants known to be pathogenic, often insufficient data exist to predict the likelihood of disease in an individual who is currently asymptomatic. Communicating this uncertainty to the clinician remains a challenge for the clinical laboratory. For example, if genomic sequencing for a 60-year-old patient with no signs, symptoms, or family history of heart disease uncovers a rare genetic variant in a known cardiomyopathy gene, the treating clinician has no data to guide her in interpreting the significance of that finding for her patient. The complexity of clinical sequencing reports might be prone to misinterpretation by nongeneticist physicians, leading to over- or underestimation of the disease risk associated with a given variant. Such results might prompt physicians to order an expensive cascade of follow-up diagnostic tests, each with its own potential complications, risks to the patient, and costs (*4*).

The concerns voiced above reflect an appropriate respect for key principles in medicine, including the avoidance of patient harm and good stewardship of limited health care resources. But at what point do they create an artificial crisis that distracts from more productive questions that might point the way forward for a new field? If physicians are not ready to use genomic medicine now, how will we know when they are? A useful thought experiment is to ask the same of other medical innovations. When did the biomedical community declare nonradiologist physicians ready to order computerized tomography (CT) scans for their patients and make clinical decisions based on their findings? Introduced in the 1970s, CT carries risks associated with radiation, intravenous contrast agents, and the discovery of radiographic lesions incidental to the test's primary indication. However, with guidance from their radiologist colleagues, physicians routinely use CT for the standard management of conditions ranging from abdominal pain and headaches to cancer and stroke.

On what grounds would we hold genomic technology to different standards? Similar to the radiologist, the genomics-laboratory director holds primary responsibility for interpreting sequencing results using available data and generating reports that physicians can understand. The receiving physicians may choose to communicate back with the specialist for further guidance in medical decision-making. As genomic medicine grows in prominence, nongeneticist physicians might also seek greater support from genetic counselors than they now do in practice.

Genetic exceptionalism is the idea that genetic technology and information are inherently different from other routine processes in medical care and, by extension, should be handled more cautiously (*5*). Additional caution might be appropriate for genetic information that is potentially stigmatizing or anxiety provoking. But like any other medical test, most genetic testing is used for diagnosis, prognosis, and therapeutics. Similarly, the degree of physician preparedness for genomic medicine is not exceptional among other complex medical innovations such as myriad types of imaging, microscopic pathology assessment, or targeted therapies.

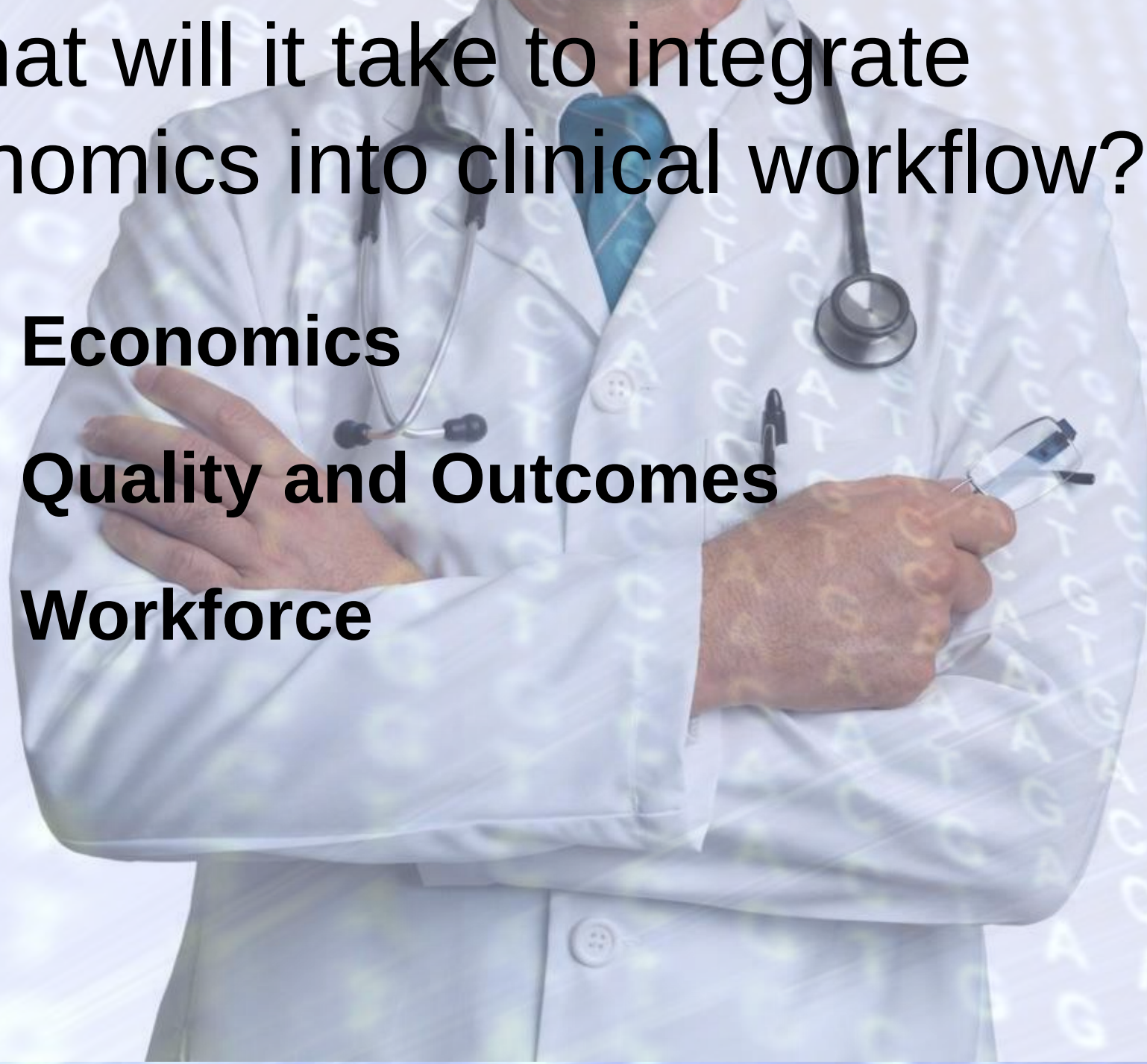
DEFINING PREPAREDNESS

The concerns about physician preparedness for genomic medicine are also problematic because no universal definition of preparedness exists. To a large extent, these concerns stem from surveys in which physicians have reported little experience with genomic medicine in their practices and low perceived confidence in their ability to order genetic tests and manage the results appropriately (*3*). But self-reported attitudes and perceptions do not necessarily correlate with skills and behavior. Even objective genomics knowledge assessment might not adequately determine whether a physician can use genomic medicine in his or her practice.

To assess residency education across the spectrum of medical specialties, the Accreditation Council for Graduate Medical Education (ACGME) has identified six core competencies that training programs should target: patient care, knowledge for practice, practice-based learning and improvement, interpersonal and communication skills, professionalism, and systems-based practice; the Association of American Medical Colleges (AAMC) has added two others: interprofessional collaboration and personal and professional development (*6*). Although these discrete competencies facilitate the evaluation of trainees, they oversimplify what it means to be an effective physician. To better describe the roles a physician plays, medical specialties are now defining entrustable professional

[1]Section of General Internal Medicine, VA Boston Healthcare System, Boston, MA 02130, USA. [2]Division of General Medicine and Primary Care, Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA. [3]Department of Medicine, Harvard Medical School, Boston, MA 02115, USA. [4]Department of Genetics, University of Alabama at Birmingham, Birmingham, AL 35233, USA. [5]Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA.
*Corresponding author. E-mail: jvassy@partners.org

What will it take to integrate genomics into clinical workflow?



- **Economics**
- **Quality and Outcomes**
- **Workforce**