Genomic Medicine: Physician Literacy in Cardiology

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Overview: Four Important Areas

- Diseases of Particular Interest to CV Medicine
- ACC – Personalized Medicine Survey
- ACC CME and MoC Offerings
- Future ACC Directions

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1 Diseases & Conditions of Particular Genetic/Genomic Interest in CV Medicine

- Mendelian CV Diseases
  - Hypertrophic Cardiomyopathy
  - Long QT Syndromes
  - Marfan Syndrome
  - Familial Dilated Cardiomyopathy
  - Factor V Leiden
- Complex Genetic Diseases
  - CAD, HTN
  - Atrial fibrillation
- Pharmacogenetics
  - Warfarin metabolism
  - Clopidogrel activation

The Current Landscape of Personalized Medicine in Cardiology: *Providers and Patients*

Source: *ACC's CardioSurve panel*

(Oct. 2010 survey of more than 150 cardiovascular professionals)

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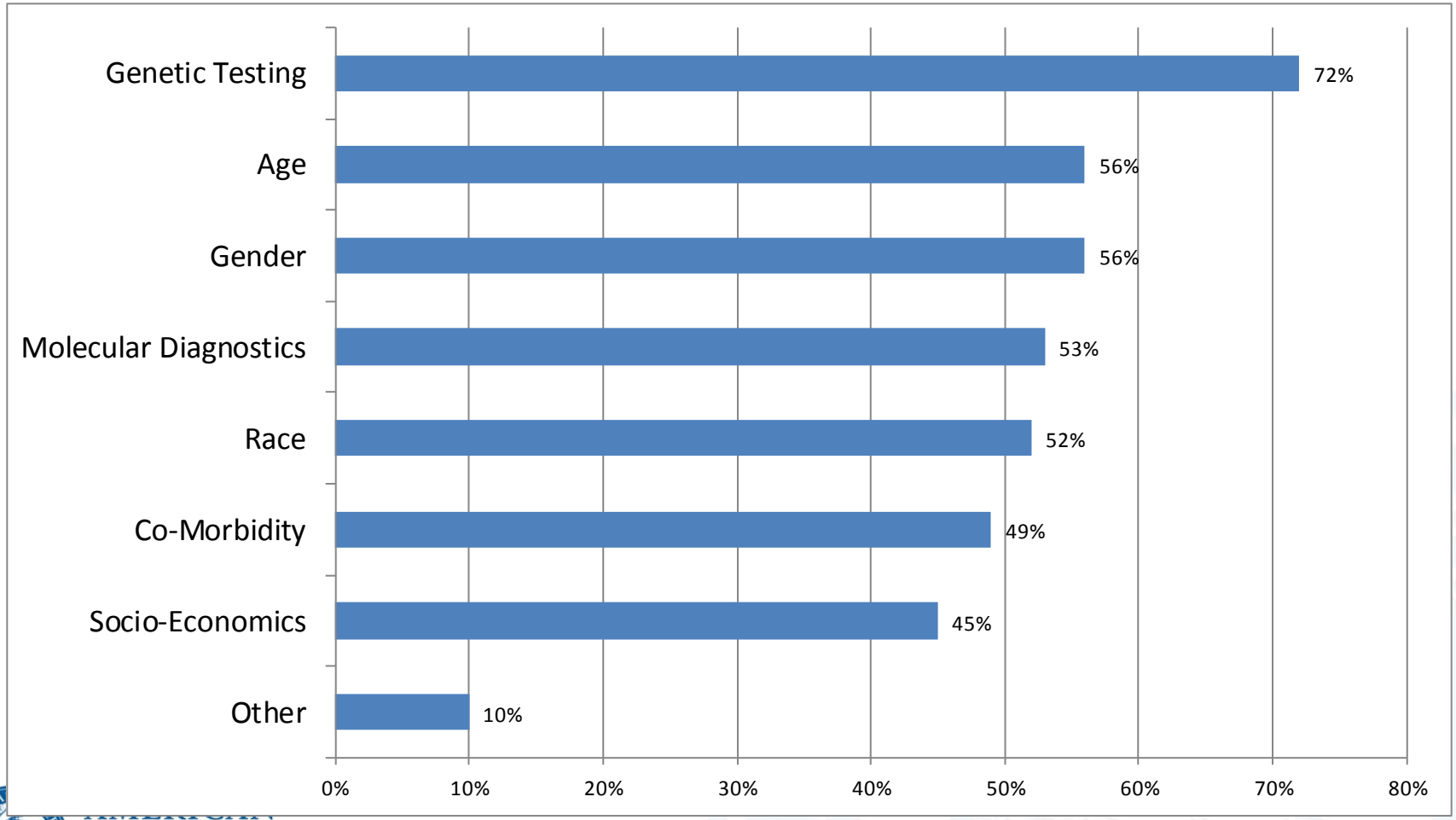
ACC Personalized Medicine Survey – 2010

What is Personalized Medicine?



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2 ACC Personalized Medicine Survey - 2010

Percent of Patients Asking Cardiologists about Personalized Medicine (n=144)	
0% of patients	33%
1% - 5% of patients	37%
6% - 10% of patients	17%
11% - 20% of patients	8%
More than 20% of patients	5%
Mean % of patients	6%

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2 ACC Personalized Medicine Survey - 2010

Percent of Patients that Cardiologists are Using Personalized Medicine (n=154)	
0% of patients	29%
1% - 5% of patients	41%
6% - 10% of patients	14%
11% - 20% of patients	9%
More than 20% of patients	7%
Mean % of patients	7%

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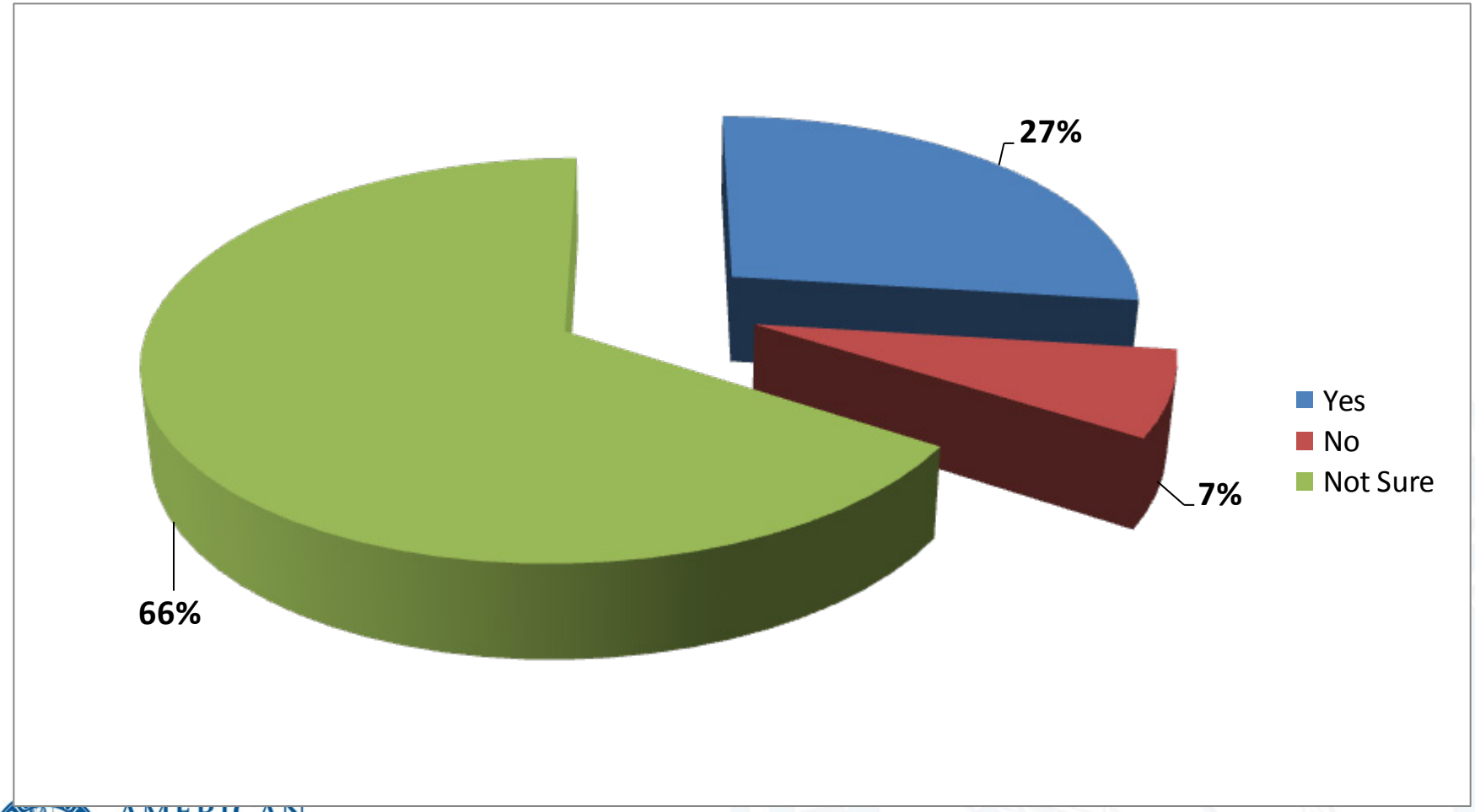
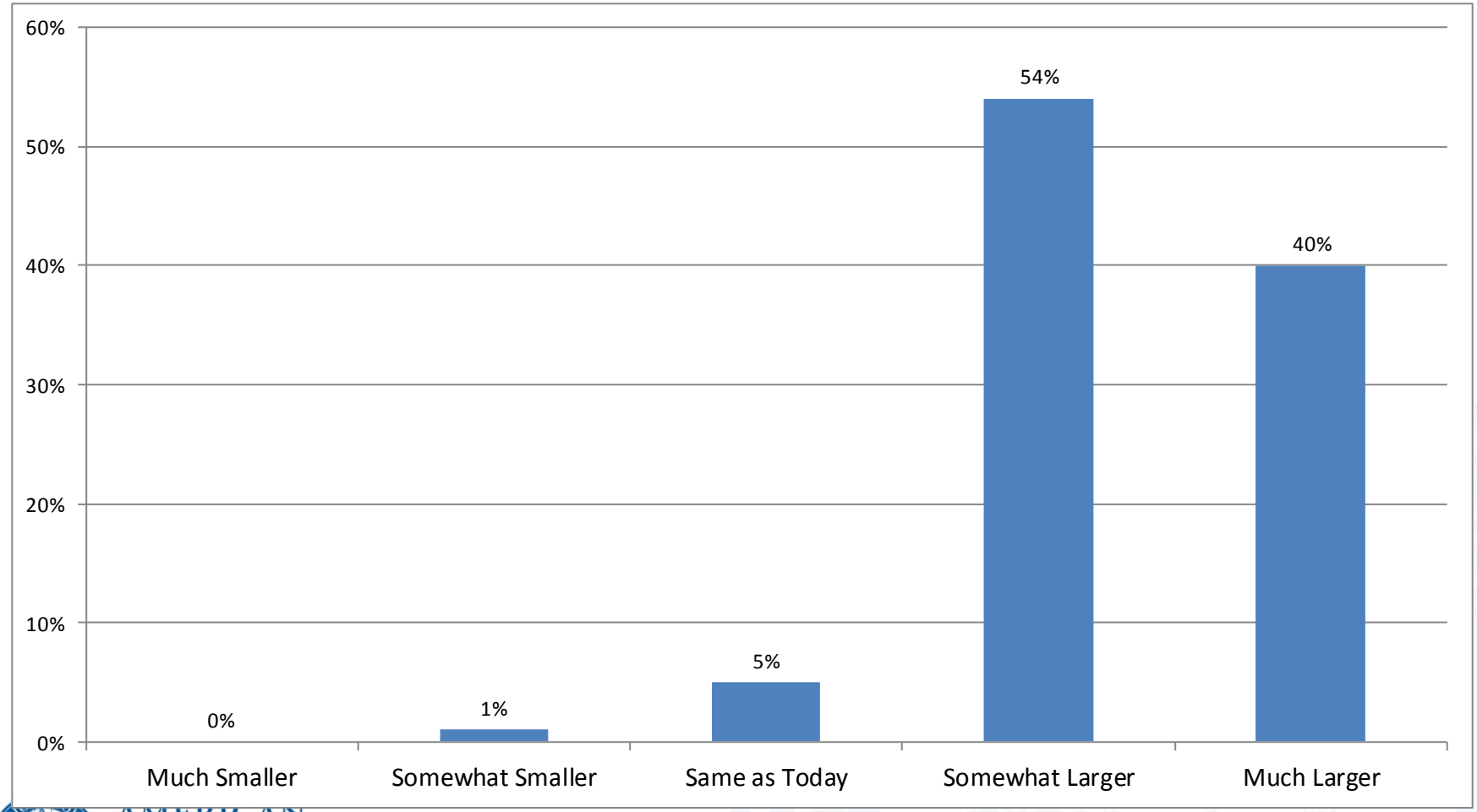
2 Future Use of Personalized Medicine



2 Future Role of Personalized Medicine



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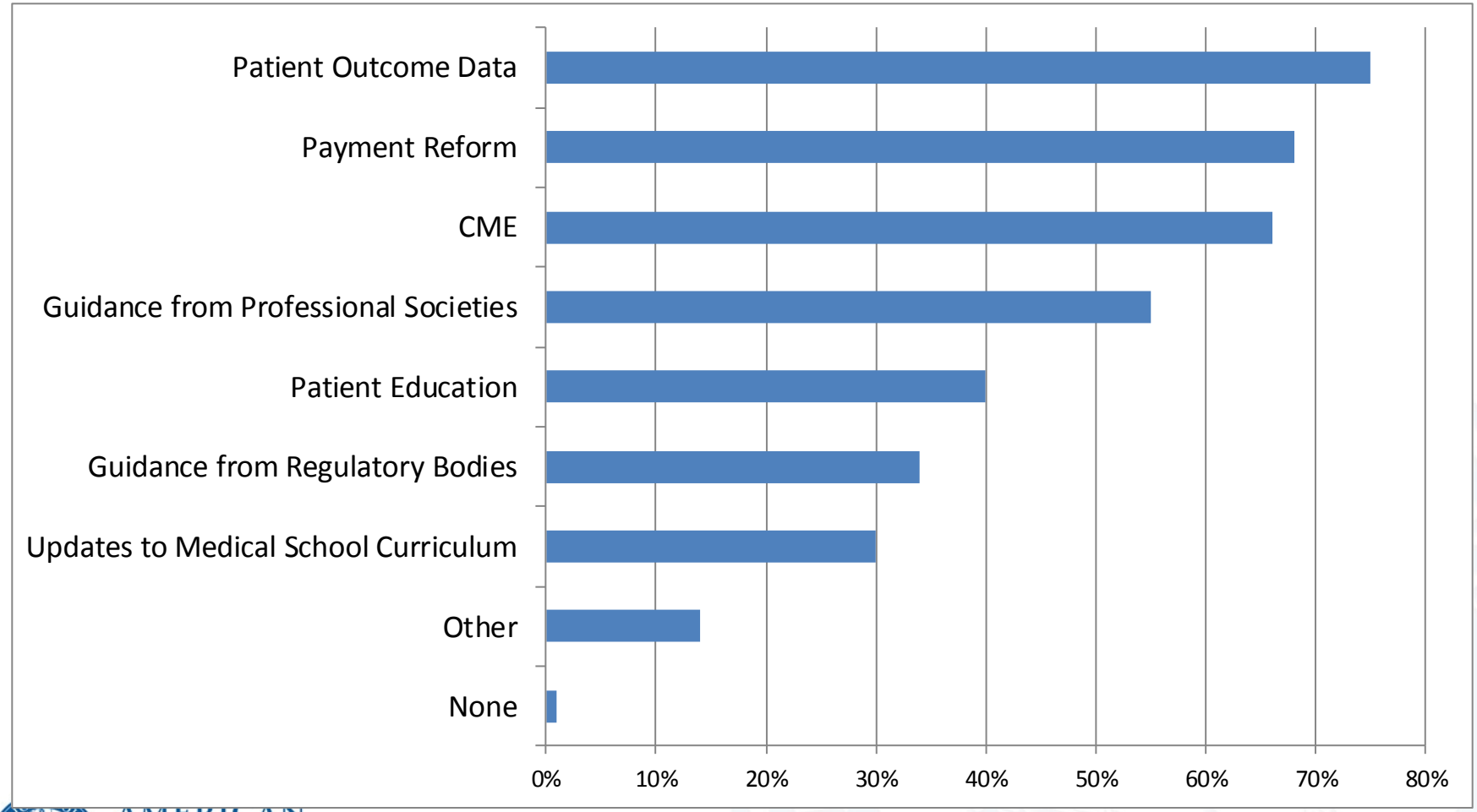
Challenges to Clinical Implementation of Personalized Medicine



Importance of Genetics in Cardiovascular Medicine: New Discoveries & Realities

January 28 2013

Presented by:

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President and CEO, University of Ottawa Heart Institute
Director, Ruddy Canadian Cardiovascular Genetics Centre

Disclosure: Potential conflicts of interest have been resolved
- Cumberland Pharmaceuticals
- Celera Corporation

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Inherited Causes of Sudden Cardiac Death

CARDIOMYOPATHIES

- Hypertrophic Cardiomyopathy (HCM)
- Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)
- Dilated Cardiomyopathy (DCM)
- Coronary Artery Abnormalities

ARRHYTHMIAS

- Long QT Syndrome (LQTS)
- Short QT Syndrome
- Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)
- Brugada Syndrome
- Wolff-Parkinson-White (WPW) Syndrome

Clinical Screening For HCM

≥12 years:

- **Family members should undergo physical examination**
- **ECG and echo at 12 to 18 month intervals**

18 to 20 years:

- **ECG and Echo every 5 years unless there is a clinical development**
- **Screening of first degree relatives are encouraged**

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Maron BJ, McKenna WJ, Danielson G, et al.
JACC 2003;42: 1687-713

Clinical Considerations

- Screening for causes of sudden cardiac death in the young
- History and physical examination detects less than 1%
- ECG exhibits abnormalities in over 80% of individuals with HCM, LQTS and WPW
- High % of false-positives

Role of Genetic Testing in Diagnosis of Cardiomyopathies

- **HCM**
- **Fabry's Disease**
- **Amyloidosis**
- **Other metabolic causes of hypertrophy**

Role of Genetic Testing in Long QT Syndrome

- Long QTS-1 (Potassium Channel KV7.1) 35%
- Long QTS-2 (Potassium Channel KV11.1) 30%
- Long QTS-3 (Sodium Channel SCN5A) 10%

Therapy

- Long QTS-1 — Beta Blockers
- Long QTS-2 } Beta Blocker plus mexiletine, flecainide or ranolazine
- Long QTS-3 }

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Benefits of Genetic Testing

- Genetic counseling
- Diagnostic
- Therapeutic implementation
- Cost effective

Sudden Death in Athletes

- **75% of all deaths in athletes is cardiac related and almost always precipitated by exertion.**
- **Familial hypertrophic cardiomyopathy (HCM) is the most common cause of sudden cardiac death below the age of 36 years.**
- **HCM is almost always asymptomatic, thus no warning precedes sudden death.**

The following professional sporting organizations endorse ECG screening followed by other tests if abnormal

- **National Football League (NFL)**
- **Major League Baseball (MLB)**
- **National Basketball Association (NBA)**
- **National Hockey League (NHL)**
- **Major League Soccer (MLS)**

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Role of Genetic Testing in Cardiovascular Pharmacogenomics

- **Anticoagulation**
- **Platelet Therapy**

9p21: The First Genetic Risk Factor For CAD

9p21 genetic risk variant is extremely common with one or two copies occurring in 75% of the population

Homozygotes carry increased risk of 50% for CAD
Heterozygotes carry increased risk of 25% for CAD

9p21 locus risk is independent of known risk factors for CAD, namely: cholesterol, hypertension or diabetes

9p21 risk allele is estimated to be present in 4.5 billion people

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McPherson R, et al. Science 2007:316(5830);1488 – 1491

Helgadottir A, et al. Science 2007:316(5846);1491-3

Genetics Of Coronary Artery Disease and Myocardial Infarction

50 genetic risk variants for CAD of genome-wide significance have been identified and replicated in independent populations

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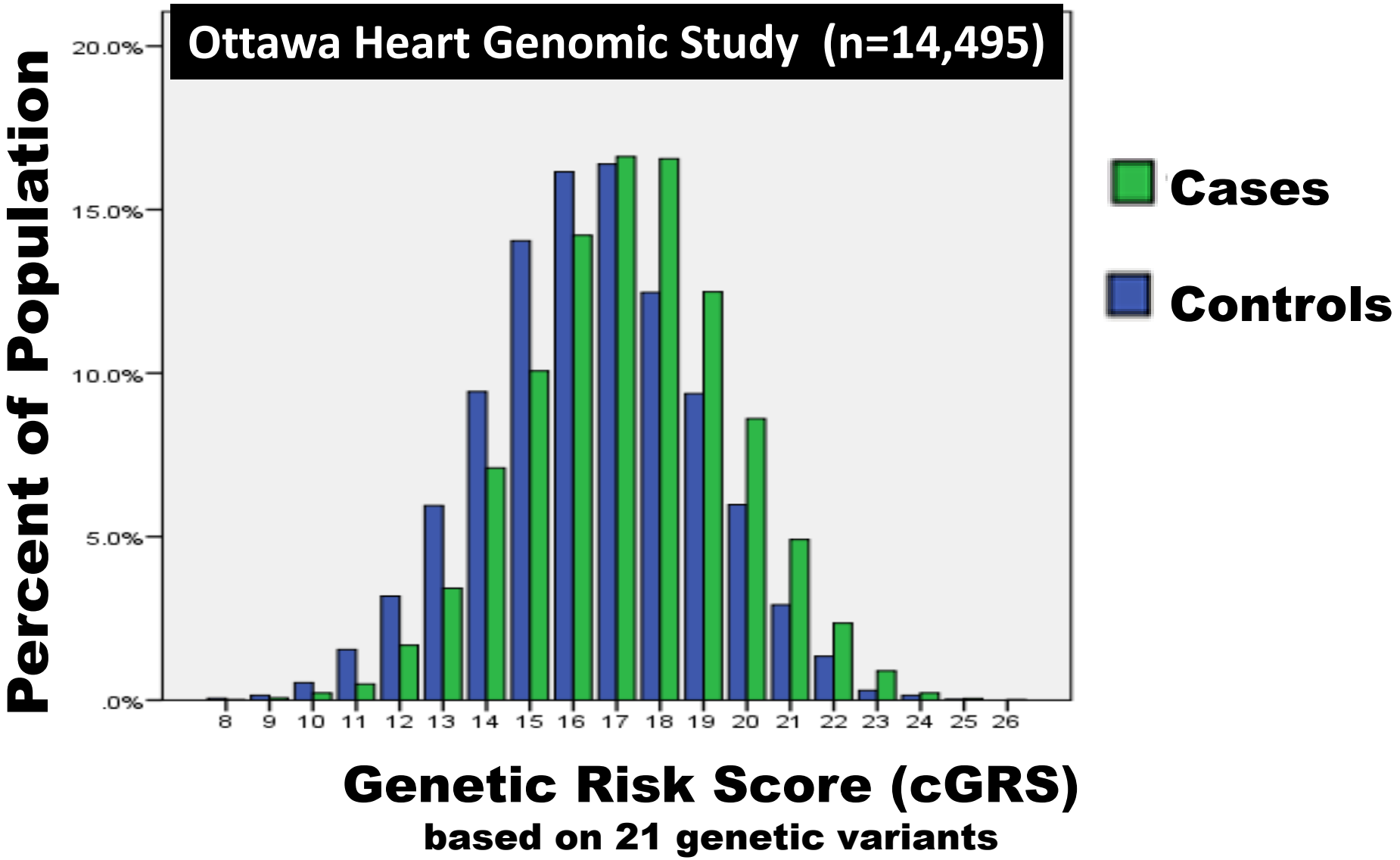
CARDIoGRAMplusC4D Consortium.
Nature Genetics: Jan 2013;Vol.45

Distribution of Genetic Risk Variants Associated with CAD



Directives for Cardiology

- The time for genetic testing of cardiovascular Mendelian disorders is now.
- Genetic screening is ultimately necessary for comprehensive prevention of Coronary Artery Disease
- Personalized Medicine is in large part dictated by genetic predisposition

Structured education of Genetics is a prerequisite to enable our cardiologists to be proactive.

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ACC Educational Offerings in Genetics/Genomics

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3 ACC CME and MoC Offerings

- ACCSAP 8 (ACC Self Assessment Program) "Cardiovascular Genetics"
  - CME and MOC (maintenance of certification) offering
  - Mendelian CV Diseases
  - Complex Genetic Diseases
  - Pharmacogenetics

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3 ACC CME and MoC Offerings

- Annual ACC Scientific Sessions
  - ACC.11
    - 3 sessions on translational research in genetics, pharmacogenetic tailored antiplatelet therapy, and functional genomics in CV disease
  - ACC.12
    - 7 sessions on personalized medicine, genome sequencing, translational research, genetic testing, gene therapy for heart failure, and the genetics of sudden cardiac death

3 ACC CME and MoC Offerings

- Live Programs – Genetic/Genomic Topics
  - 2011
    - "Genetics and genomics"
    - "Careers in Genetics and Proteomics"
  - 2012
    - "Addressing LV Dysfunction by Gene Therapy Upgrading of Metabolism"
    - "Genetics and Arrhythmias"

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New Lifelong Learning & MOC

ACC Cardiosource

Helping Card
Learn. Advan

ACC Digital Strategy

Optimize Delivery of Knowledge & Decision Support tools

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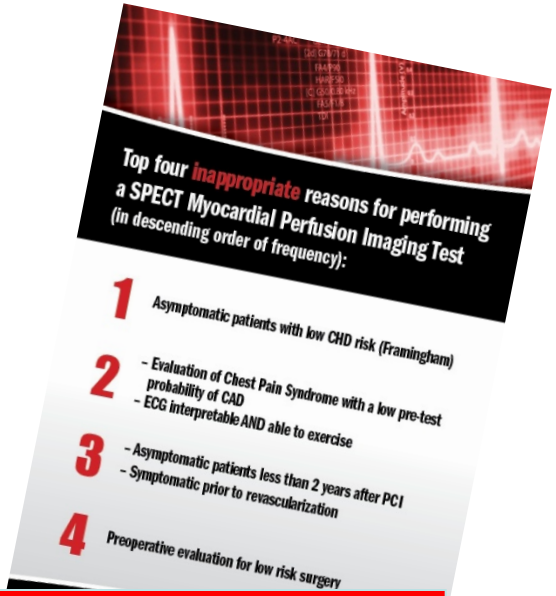
Appropriate Use Criteria (AUC)

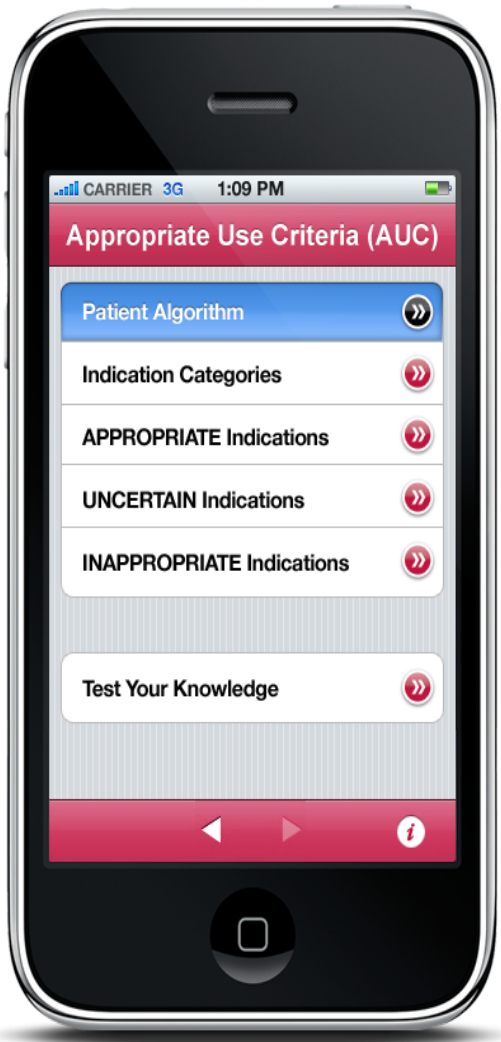
- SPECT-MPI
- CCT/MRI
- TTE/TEE
- Stress Echocardiography
- Coronary Revascularization: PCI/CABG
- SPECT-MPI Update



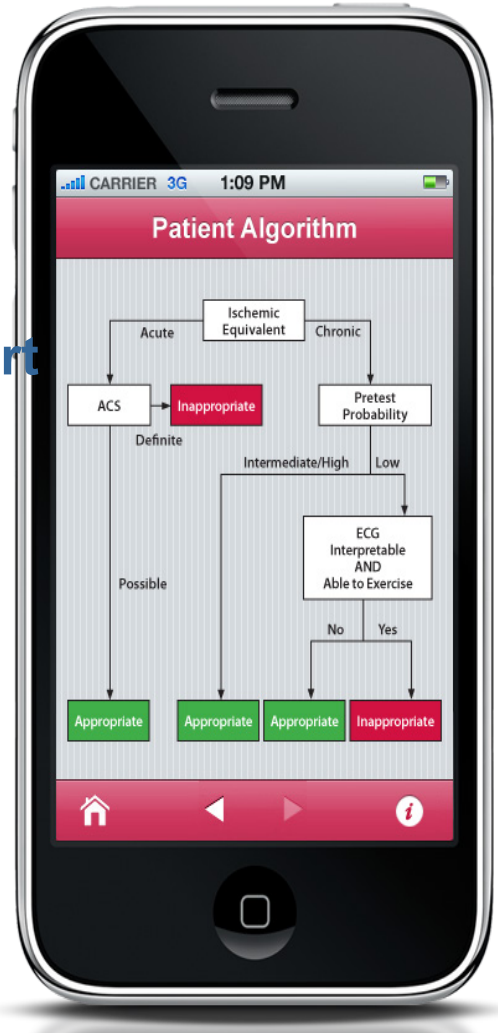
Imbed Appropriateness of Genetic testing in Disease Entities & Clinical Scenarios?

- Pacemaker/ICD (2013)
- Multimodality (2013)

Knowledge & Decision Support Tools at the Point of Care



- Migration towards point-of-order
- Embedded clinical decision support
- Tracking/data registry
- Reporting/feedback



4 Future ACC Direction

ACC BoT Basic Science Advisory Task Force

- Dr. Geoffrey Ginsberg (Chair)
- Dr. Thomas Caskey
- Dr. Robert Roberts
- Dr. Christine Siedman
- Dr. Jennifer Hall
- Dr. Pat O'Gara
- Dr. Deepak Srivastava

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Future Goals

- To develop whitepapers on basic and translational science anticipated to affect cardiovascular practice in the next 10 years.
- To recommend goals for training the next generation of cardiologists (in training and early career) as well as at the current practitioner based on the emerging science and technologies that will impact the practice of cardiovascular medicine
- To advise the ACC on scientific questions, research strategy, and partnerships with other organizations.

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“It’s far more important to know what person the disease has than what disease the person has.”

– *Hippocrates*

Thank You

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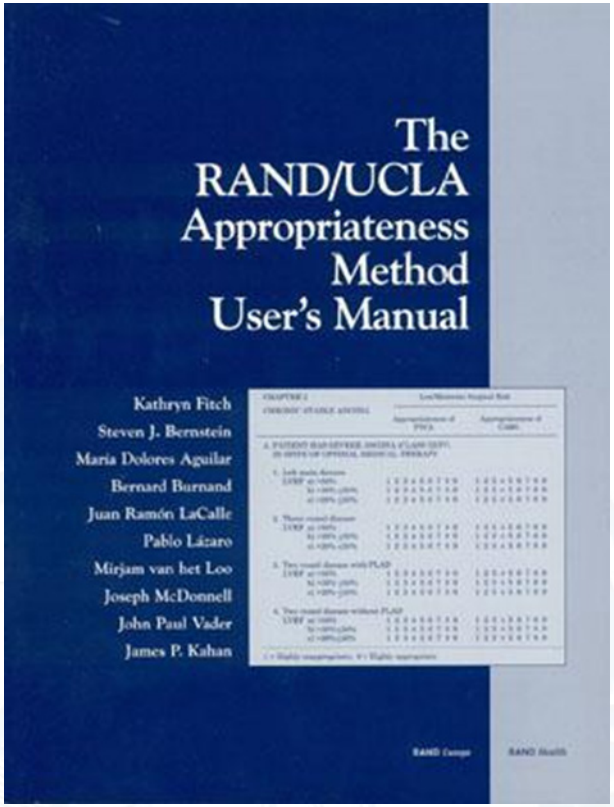
Appropriate Use Criteria (AUC)

Define the “when to do” and “how often to do” a test or procedure in the context of scientific evidence, the health care environment, the patient’s profile and a physician’s judgment



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