A Scientific Foundation for Using Personal Genomics for Risk Assessment and Disease Prevention

Muin J. Khoury MD, PhD

CDC Office of Public Health Genomics

NCI Senior Consultant in Public Health Genomics

Perspective

JANUARY 10, 2008

NEJM

Letting the Genome out of the Bottle — Will We Get Our Wish?

David J. Hunter, M.B., B.S., Sc.D., M.P.H., Muin J. Khoury, M.D., Ph.D., and Jeffrey M. Drazen, M.D.

It may happen soon. A patient, perhaps one you have known for years, who is overweight and does not exercise regularly, shows up in your office with an analysis of his whole genome at multiple single-nucleotide polymorphisms types. These studies rely on mi-

The test undergone by the patient described above is one of the products of this new knowledge.

As of November 2007, two companies have made available direct-to-consumer "personal genome services" (www.23andme.

Outline

- Personal genomics 2009
- A scientific foundation for personal genomics
- Recommendations of NIH-CDC workshop December 2008

Are we There Yet?

PERSPECTIVE

COMMON GENETIC VARIATION AND HUMAN TRAITS

Common Genetic Variation and Human Traits

David B. Goldstein, Ph.D.

The human genome has been ... only slightly a gene's expression ... would collectively generate a sub-

PERSPECTIVE

GENOMEWIDE ASSOCIATION STUDIES — ILLUMINATING BIOLOGIC PATHWAYS

Genomewide Association Studies — Illuminating Biologic Pathways

Joel N. Hirschhorn, M.D., Ph.D.

Human geneticists ... seek ... to understand the ... sis of human biology ... aiming either to gain ... could eventually impr... or to produce usefu... or predictive tests. A... 2004, few genetic v...

Genetic Risk Prediction — Are We There Yet?

Peter Kraft, Ph.D., and David J. Hunter, M.B., B.S., Sc.D., M.P.H.

A major goal of the Human Genome Project was to facilitate the identification of inherited genetic variants that increase or decrease the risk of complex diseases. The completion of the International HapMap Project and the development of new methods for genotyping individual DNA samples at 500,000 or more loci ... tests of genetic predisposition to important diseases would have major clinical, social, and economic ramifications. But the great majority of the newly identified risk-marker alleles confer very small relative risks, ranging from 1.1 to 1.5,[2] even though such analyses meet stringent statistical criteria (i.e., the identification of associa- ... est relative risks are almost certainly overrepresented in the first wave of findings from genome-wide association studies, since considerations of statistical power predict that they will be identified first. However, a striking fact about these first findings is that they collectively explain only a very small proportion of the

"Should the Perfect be the Enemy of the Good?"

- "One argument in favor of using the available genetic predictors is that same information is better than no information, and we should not let the perfect be the enemy of the good by refusing to make use of our knowledge until it is more complete. Why not begin testing for common genetic variants whose associations with susceptibility to disease have been established?"

- Kraft P and Hunter D. NEJM 2009;360:1701.

2008: Invention of the Year

TIME's Best Inventions of 2008

Invention of the Year

Next

1. The Retail DNA Test

By Anita Hamilton

ARTICLE TOOLS
Print
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Sphere
AddThis
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Yahoo! Buzz

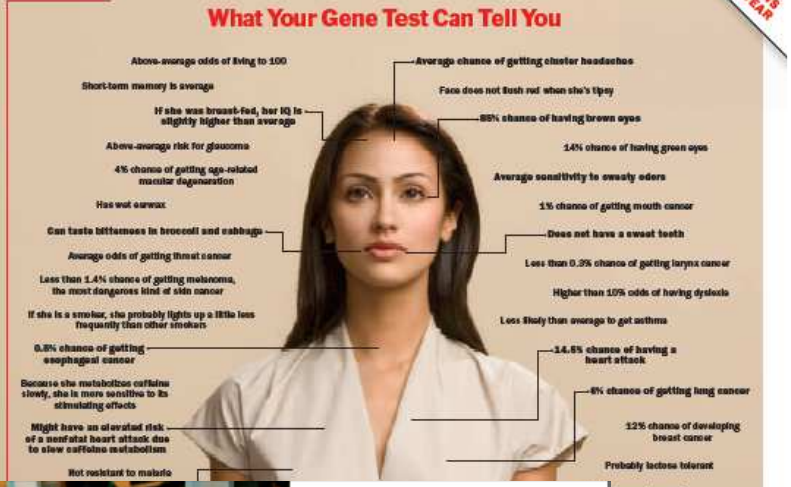
Before meeting with Anne Wojcicki, co-founder of a consumer gene-testing service called 23andMe, I know just three things about her: she's pregnant, she's married to Google's Sergey Brin, and she went to Yale. But after an hour chatting with her in the small office she shares with co-founder Linda Avey at 23andMe's headquarters in Mountain View, Calif., I know some things no Internet search could reveal: coffee makes her giddy, she has a fondness for sequined shoes and fresh-baked bread, and her unborn son has a 50% chance of inheriting a high risk for Parkinson's disease.

Learning and sharing your genetic secrets are at the heart of 23andMe's service — a $399 saliva test that estimates your predisposition for mor conditions ranging from baldness to blindness. Although 23andMe isn't selling DNA tests to the public, it does the best job of making them acc affordable. The 600,000 genetic markers that 23andMe identifies and

THE BEST INVENTIONS OF THE YEAR

Invention Of the Year

Your genome used to be a closed book. Now a simple, affordable test can shed new light on everything from your intelligence to your biggest health risks. Say hello to your DNA— if you dare



IN DEPTH

Inflated expectorations: At a September "spit party" hosted by 23andMe, invitees supply samples for free genetic testing

And they must be able to analyze genetic data in light of each individual's entire medical history, including lifestyle choices and environmental exposures.

Consider the case of Mike Spear, communications director for Genome Alberta, a Canadian nonprofit. He recently got his genes read by 23andMe. "One of the things that stood out

Time, November 10, 2008

Proliferation of Personal Genomic Tests

Genome wide	GWAS platforms Whole sequencing	23andme, decodeME, Navigenics Knome
Selected variants	Specific diseases or traits	Proactive Genetics, DNA Direct, Genelex
Other	Ancestry, nutritional, dermatologic, athletic	FamilyTree DNA Dermatogenetics, sciona, suracell

K Offitt JAMA March 19, 2008

Proliferation of Personal Genomic Tests

The American Journal of BIOETHICS

JOURNAL ARTICLES

Volume 9 Number 7
July 2009

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Social Networkers' Attitudes Toward Direct-to-Consumer Personal Genome Testing

by Amy McGuire, Christina M Diaz, Susan G Hilsenbeck, Tao Wang
2009. *The American Journal of Bioethics* 9(7):3

Abstract/Extract

Purpose: To explore social networkers' interest in and attitudes toward personal genome testing (PGT) and its clinical integration.

Methods: An online survey of 1,087 social networkers was conducted. Descriptive statistics were calculated to summarize respondents' characteristics and responses.

Results: 6% of respondents have used PGT, 64% would consider using PGT, and 30% would not use PGT. Of those who would consider using PGT, 74% would use it to gain knowledge about disease in their family and 78% would ask their physician to help interpret test results. 61% of all respondents believe physicians have a professional obligation to help interpret results and 34% consider PGT results a medical diagnosis.

Conclusion: Respondents express interest in using
related to medical care and expect physicians to he
Physicians should be prepared for patient demands
on the basis of PGT results.

FULL TEXT

It's Your Data ... Shouldn't You Have Access To It?

Posted Thu, 02/07/2009 - 16:36 by Robert Hastings

Interesting little piece from 23andme about individual data rights

Related Links

- It's Your Data ... Shouldn't You Have Access To It?
- Health Data Rights

Average:

Public Awareness and Use of DTC Personal Genetic Tests: Results of National Healthstyles Survey 2008

- Healthstyles 2008 (5399): 77% participation
- 68% whites, 12% AA, 12% Hispanics
- 22% awareness
- 0.3% use-2/3 share results with providers
- Predictors: age, gender, education, race/ethnicity

  - From Kolor K et al, Genetics in Medicine 2009 (August)

Provider Awareness and Practices Re DTC Personal Genetic Tests: Results of National Docstyles Survey 2008

- Docstyles 2008 (1880): 510 family docs, 490 internists, 250 pediatricians, 250 Ob/Gyns
- 42% aware , 42% of whom patients had queries
- 15% one or more patients brought test results for discussion
- Of these 75% changed some aspect of practice
- Main limitation: 22% participation rate

- From Kolor K et al, Genetics in Medicine 2009 (August)

Outline

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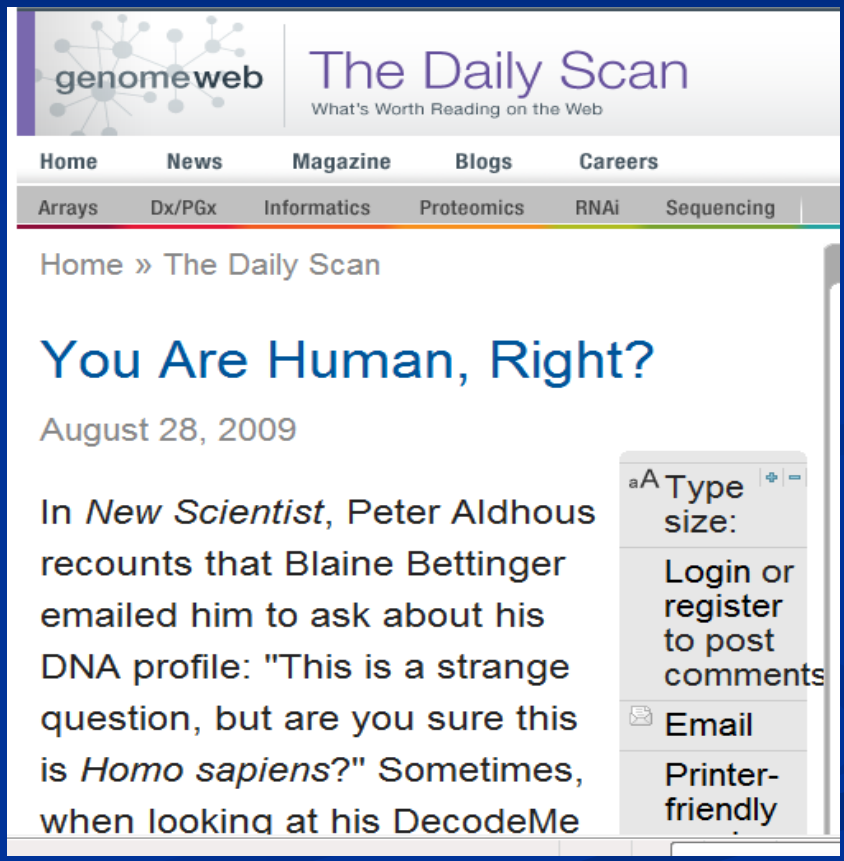
- A scientific foundation for personal genomics
- Recommendations of NIH-CDC workshop December 2008

Multidisciplinary Evaluation of Personal Genomics

- Each intended use
- ACCE Framework
- Four components
  - Analytic Validity
  - Clinical Validity
  - Clinical Utility
  - ELSI



Multidisciplinary Evaluation of Personal Genomics

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Risk assessment: odds ratios, attributable risk

Sensitivity

Specificity

Positive predictive value

Negative predictive value

Steps in Clinical Validity

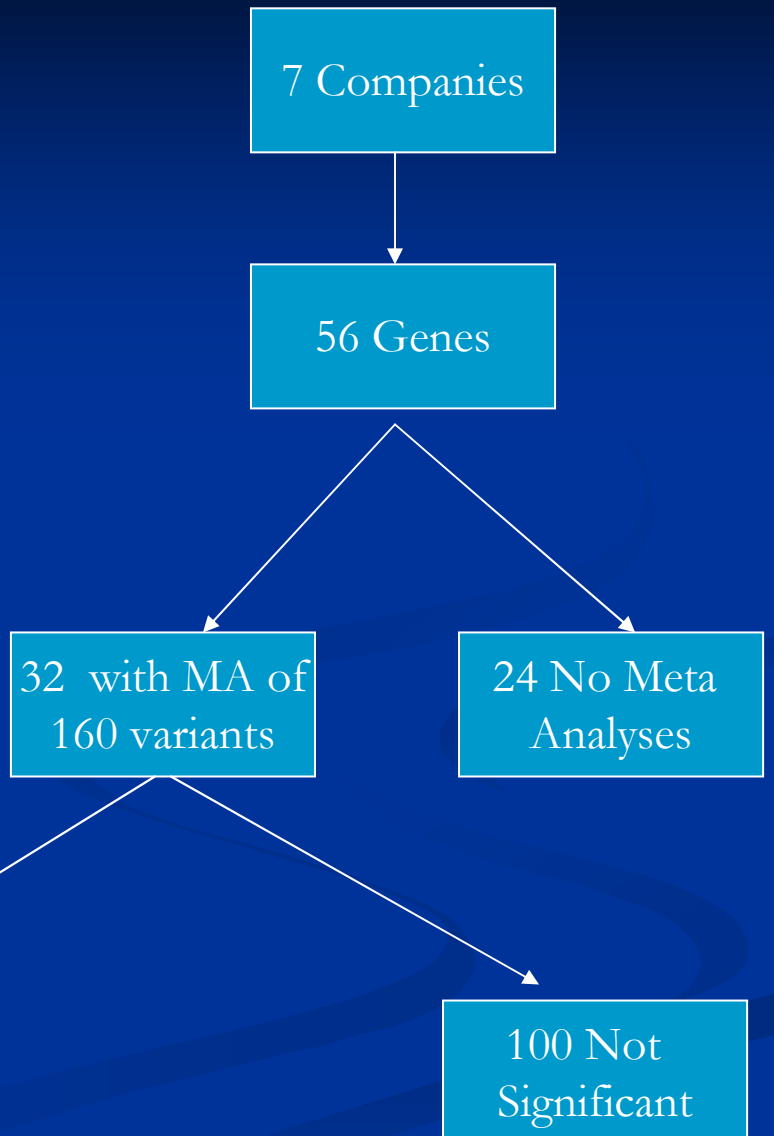
- Establishing credible genetic associations
- The uncertainty of risk estimation
- Evaluating the clinical relevance of associations

Am J Hum Genet March 2008 **ARTICLE**

A Critical Appraisal of the Scientific Basis of Commercial Genomic Profiles Used to Assess Health Risks and Personalize Health Interventions

A. Cecile J.W. Janssens,[1,*] Marta Gwinn,[2] Linda A. Bradley,[2] Ben A. Oostra,[3] Cornelia M. van Duijn,[4] and Muin J. Khoury[2]

Predictive genomic profiling used to produce personalized nutrition and other lifestyle health recommendations is currently offered directly to consumers. By examining previous meta-analyses and HuGE reviews, we assessed the scientific evidence supporting the purported gene-disease associations for genes included in genomic profiles offered online. We identified seven companies that offer predictive genomic profiling. We searched PubMed for meta-analyses and HuGE reviews of studies of gene-disease associations published from 2000 through June 2007 in which the genotypes of people with a disease were compared with those of a healthy or general-population control group. The seven companies tested at least 69 different polymorphisms in 56 genes. Of the 56 genes tested, 24 (43%) were not reviewed in meta-analyses. For the remaining 32 genes, we found 260 meta-analyses that examined 160 unique polymorphism-disease associations, of which only 60 (38%) were found to be statistically significant. Even the 60 significant associations, which involved 29 different polymorphisms and 28 different diseases, were generally modest, with synthetic odds ratios ranging from 0.54 to 0.88 for protective variants and from 1.04 to 3.2 for risk variants. Furthermore, genes in cardiogenomic profiles were more frequently associated with noncardiovascular diseases than with cardiovascular diseases, and though two of the five genes of the osteogenomic profiles did show significant associations with disease, the associations were not with bone diseases. There is insufficient scientific evidence to conclude that genomic profiles are useful in measuring genetic risk for common diseases or in developing personalized diet and lifestyle recommendations for disease prevention.



Odds Ratios 0.54-0.88 for protective variants
Odds Ratio 1.04-3.2 for risk factor variants

Steps in Clinical Validity

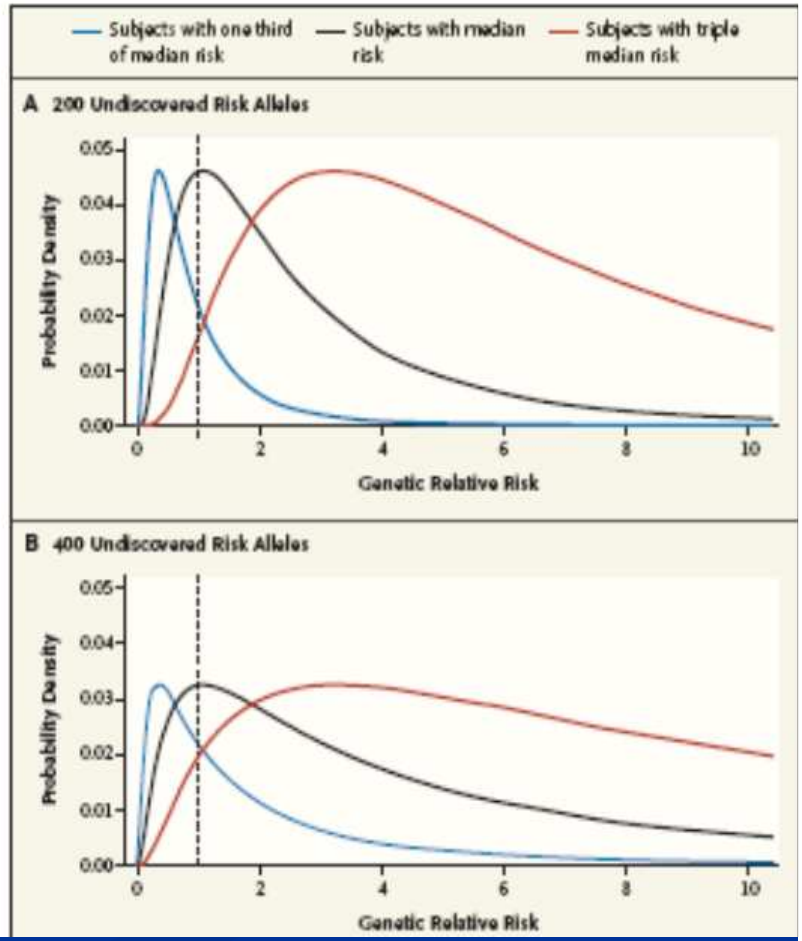
- Establishing credible genetic associations
- The uncertainty of risk estimation
  - The problem of hidden heritability
  - Gene-environment interaction
  - Biological mechanisms: pathways, gene expression, epigenomics, and so on
  - Variations in the epidemiology of the condition to be predicted (incidence, trends, allele frequency, age at testing, etc…)

The Problem of Hidden Heritability

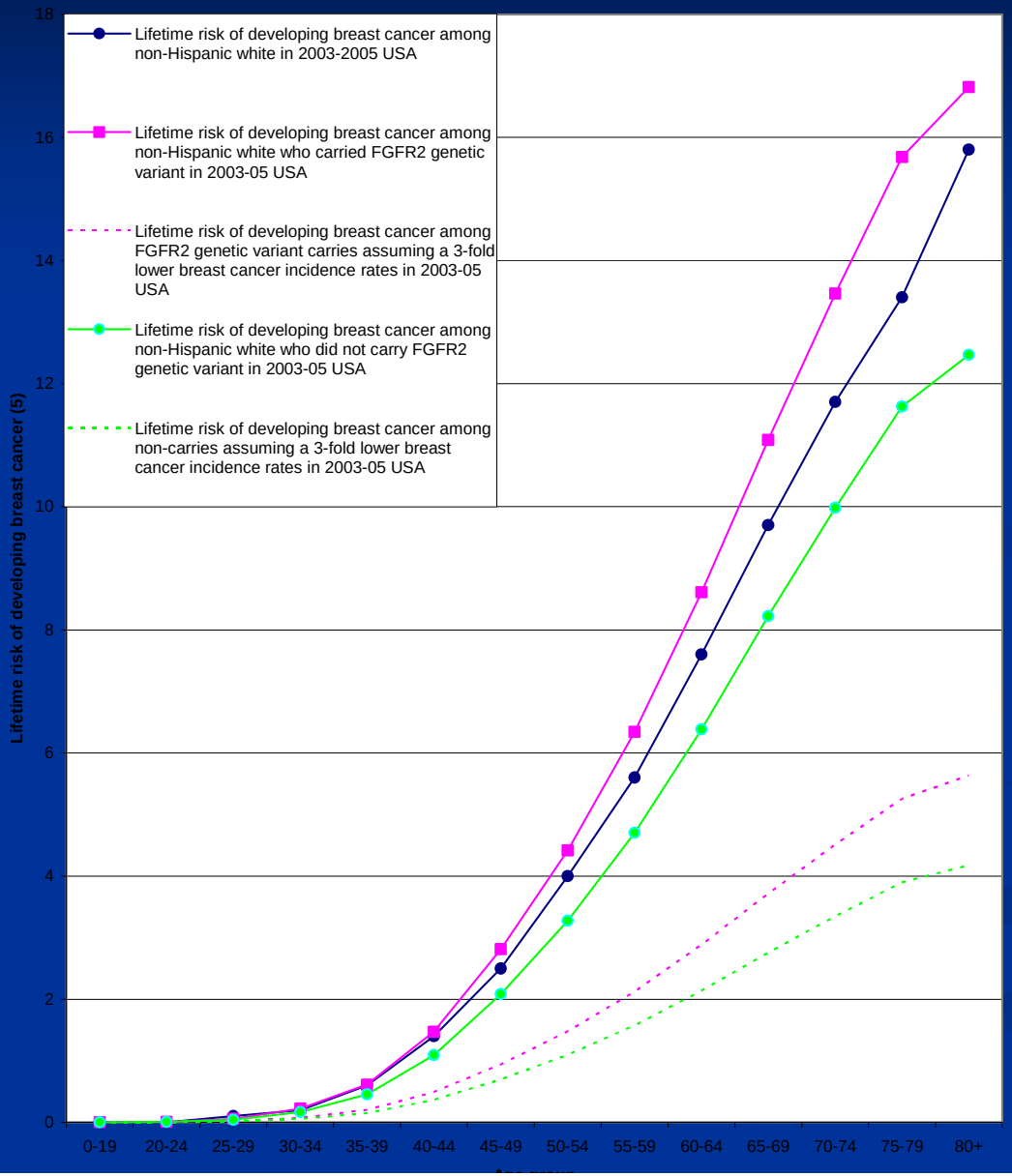
Number of Risk Alleles Needed to Produce a Sibling Relative Risk of 1.5, 2.0, or 3.0.*

Relative Risk Per Allele	Sibling Relative Risk		
	1.5	2.0	3.0
		no. of risk alleles	
1.10	203–507	347–867	550–1374
1.20	51–135	87–231	138–367

* The number of risk alleles was calculated over a range of allele frequencies (10 to 90%); the minimum and maximum numbers are presented. All alleles were assumed to have the same frequency and relative risk and to be independent.



Variations in the Epidemiology of the Disorder to be Predicted



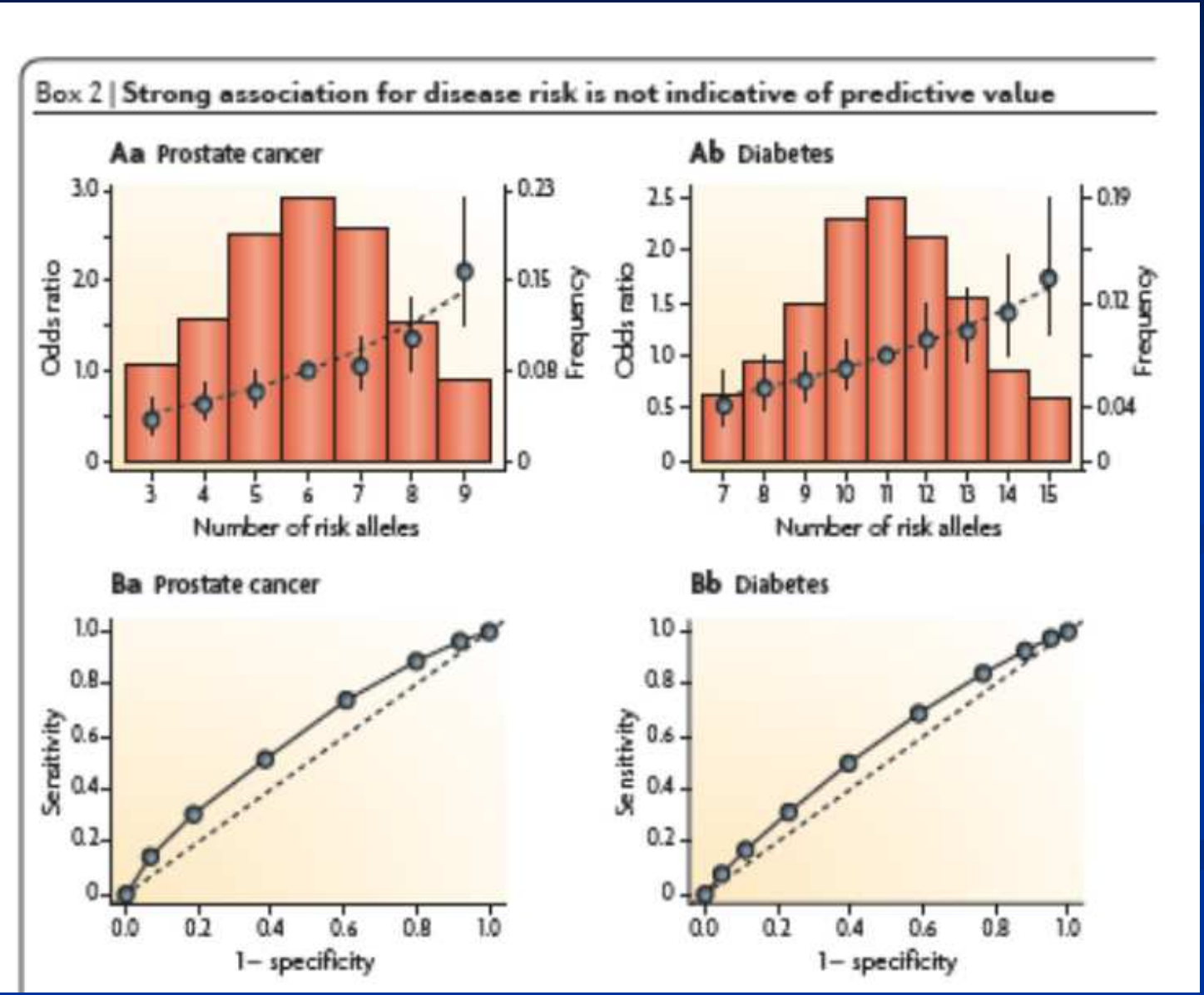
Yang Q et al, in press

Steps in Clinical Validity

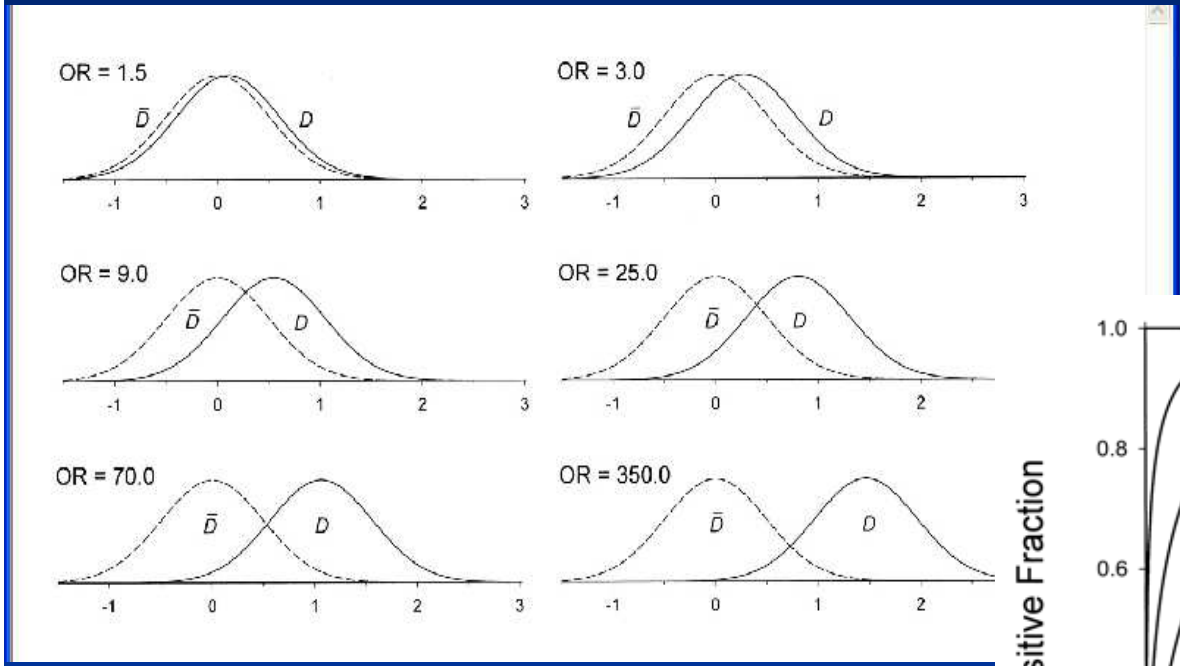
- Establishing credible genetic associations
- The uncertainty of risk estimation
- Evaluating the clinical relevance of associations
  - Measures of sensitivity, specificity and predictive values
  - Added clinical value compared to other risk factors

Genetic Associations: Beyond Odds Ratios

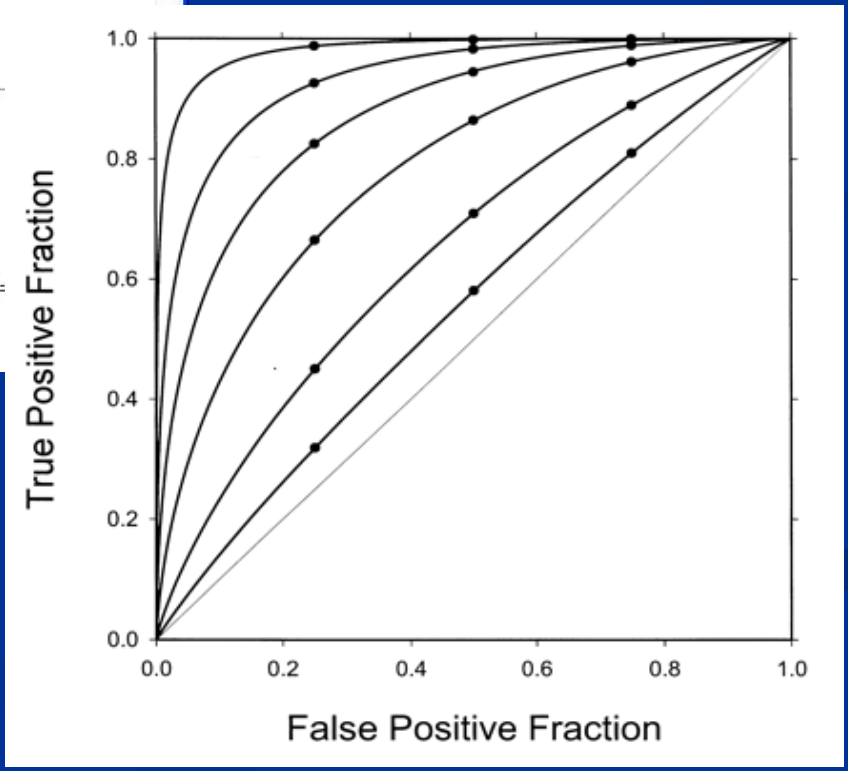
Kraft P et al. Nat Rev Genetics 2009



Association vs. Classification: Relation Between Genetic Associations and Clinical Validity of Testing for Genetic Risk Factors



AUC Analysis



Pepe et al. Am J Epidemiol 2004;159:882

Multiple Genetic Variants and Testing for Susceptibility to Various Diseases
Added Value to Traditional Risk Factors?

Year	Researchers	Disease	Genetic variant	AUC	Δ AUC
2005	Lyssenko et al.	Type 2 diabetes	3 establ. variants	0.68	+0.00
2006	Podgoreanu et al.	MI after surgery	3 (out of 48)	0.70	+0.06
2007	Humphries et al.	CHD	4 (out of 12)	0.66	+0.04
2007	Morisson et al.	CHD	11 (out of 116)	0.76	+0.01
2008	Vaxillaire et al.	Type 2 diabetes	3 (out of 19)	0.82	+0.00
2008	Zheng et al	Prostate cancer	5 (out of 16)	0.61	+0.02
2008	Kathiresan et al.	CVD	9 (out of 11)	0.80	+0.00
2008	Lango et al.	Type 2 diabetes	18 establ. variants	0.78	+0.02
2008	Van Hoek et al.	Type 2 diabetes	18 establ. variants	0.66	+0.02
2008	Meigs et al.	Type 2 diabetes	18 establ. variants	0.90	+0.00
2008	Lyssenko et al	Type 2 diabetes	11 establ. variants	0.74	+0.01

Janssens & van Duijn *Hum Mol Genet* 2008

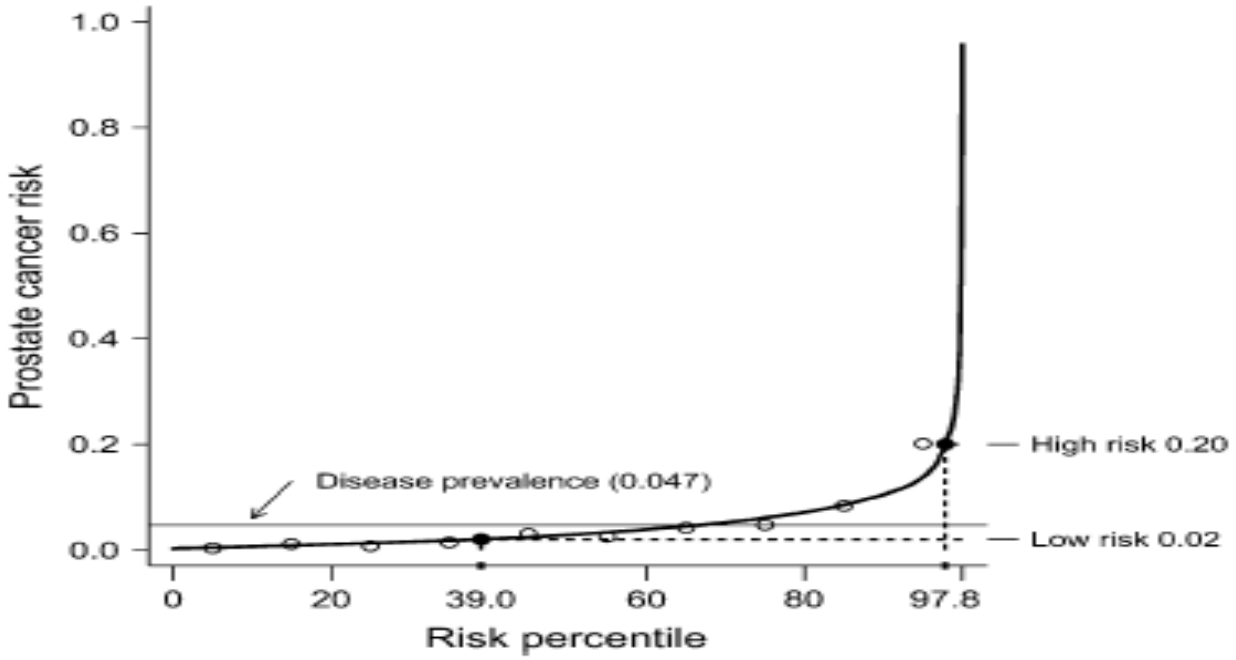
How About Risk Reclassification?

American Journal of Epidemiology
Vol. 167, No. 3
DOI: 10.1093/aje/kwm305
Advance Access publication November 2, 2007

Practice of Epidemiology

Integrating the Predictiveness of a Marker with Its Performance as a Classifier

Margaret S. Pepe[1,2], Ziding Feng[1], Ying Huang[2], Gary Longton[1], Ross Prentice[1], Ian M.



Addition of 9p21 variant to ARIC prospective cohort can lead to MI risk reclassification

Ariel Brautbar; Christie Ballantyne; Kim Lawson; Vijay Nambi; Lloyd Chambless; Aaron Folsom; James Willerson; Eric Boerwinkle

			Classification using ACRS + 9p21 allele				
			Classification using ACRS alone (percent of total cohort)				
Category			0–5%(%*)	5–10%(%*)	10–20%(%*)	>20%(%*)	
Total number reclassified for category (%*)							
10-year risk 0–5%	**Low**	3,428	3,237	191 (5.6)	0	0	191 (5.6)
Observed event rate†			*2.3*	*3.9*	*0*	*0*	*2.4*
10-year risk 5–10%	**Intermediate**	2,328	165 (7.1)	1,878	285 (12.2)	0	450 (19.3)
Observed event rate			*4.98*	*6.1*	*10.6*	*0*	*6.7*
10-year risk 10–20%	**Intermediate-high**	2,641	0	184 (7)	2,194	263 (10)	447 (17)
Observed event rate			*0*	*9.3*	*12.6*	*16.2*	*12.76*
10-year risk >20%	**High**	1,607	0	0	135 (8.4)	1,472	135 (8.4)
Observed event rate					*13.7*	*22.61*	*21.86*
	TOTAL	10,004	3,402	2,253	2,614	1,735	
Observed event rate		*1349*	*2.5*	*6.2*	*12.5*	*22*	*9.2*

*** Percentage of individuals reclassified from ACRS based risk model after adding 9p21 allele to risk calculation. † Observed event rate have been extrapolated to 10-year rate (number of events per 100 people per 10 years of observation) from a follow up time of 14.6 years. Conclusion:** The addition of the 9p21 allele to traditional risk factors, in the white population of the ARIC study, improved CHD risk prediction and reclassified a number of subjects, especially in the intermediate and intermediate-high risk categories. For the majority of the reclassified individuals, target LDL-C levels would be changed, thus altering therapy

Credible Risk Reclassification for Clinical Action

- Risk assessment models should assess
  - Calibration: correctly predicting the risk of disease within groups
  - Discrimination: correctly classifying those w/wo disease (or risk of future disease)
  - Reclassification: risk levels should cross threshold for clinical action

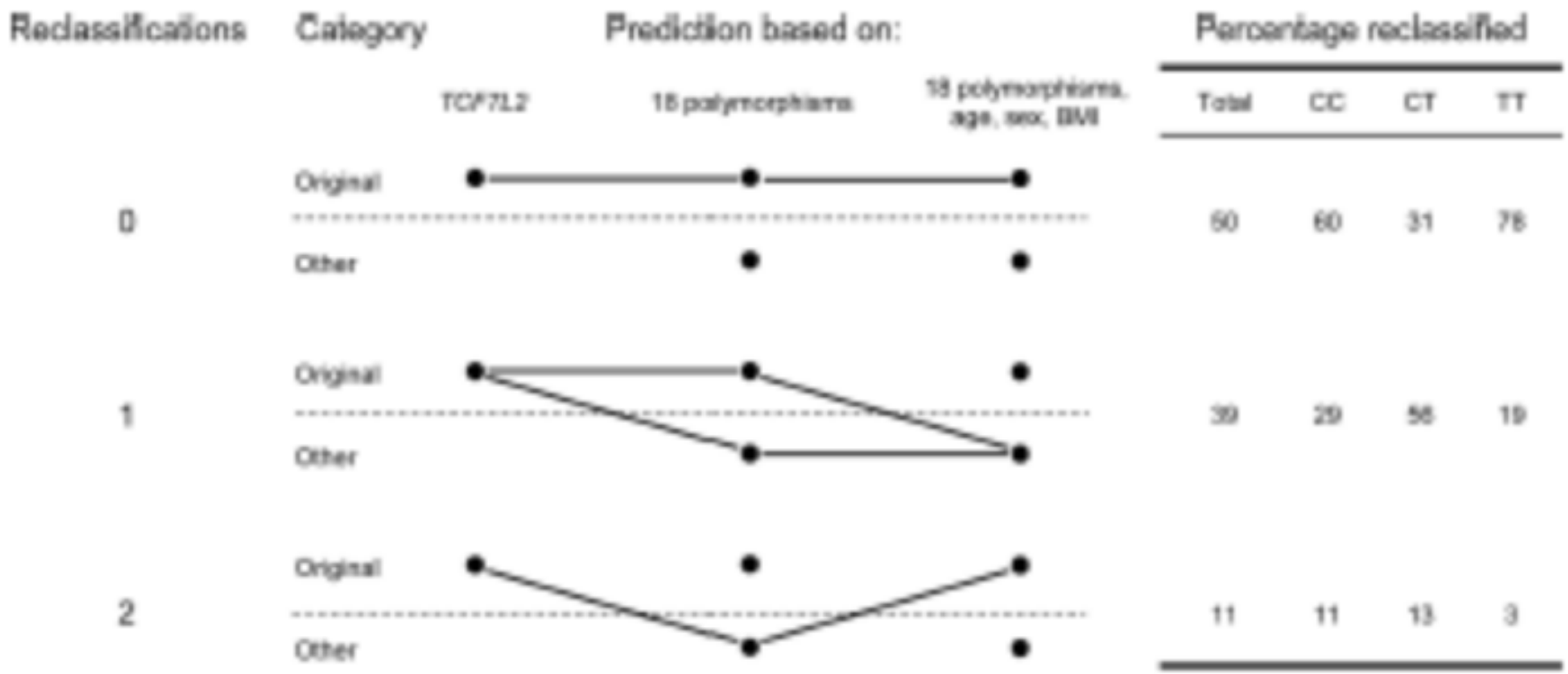
Genetics in Medicine Aug 2009

Evaluation of risk prediction updates from commercial genome-wide scans

Raluca Mihaescu, MD[1], Mandy van Hoek, MD[1,2], Eric J. G. Sijbrands, MD, PhD[2], André G. Uitterlinden, PhD[2], Jacqueline C. M. Witteman, PhD[1], Albert Hofman, MD, PhD[1], Cornelia M. van Duijn, PhD[1], and A. Cecile J. W. Janssens, PhD[1]

Purpose: Commercial internet-based companies offer genome-wide scans to predict the risk of common diseases and personalize nutrition and lifestyle recommendations. These risk estimates are updated with every new gene discovery. **Methods:** To assess the benefits of updating

offer online genetic tests to predict an individual's risk of common diseases.[6] These tests are based on single susceptibility genes (e.g., DNA direct[7]); based on genetic profiles using a limited number of variants (e.g., Sciona[8] and Genovations[9]), or genome-wide scans (e.g., 23andMe,[10] Navigenics,[11] and de-



Multidisciplinary Evaluation of Personal Genomics

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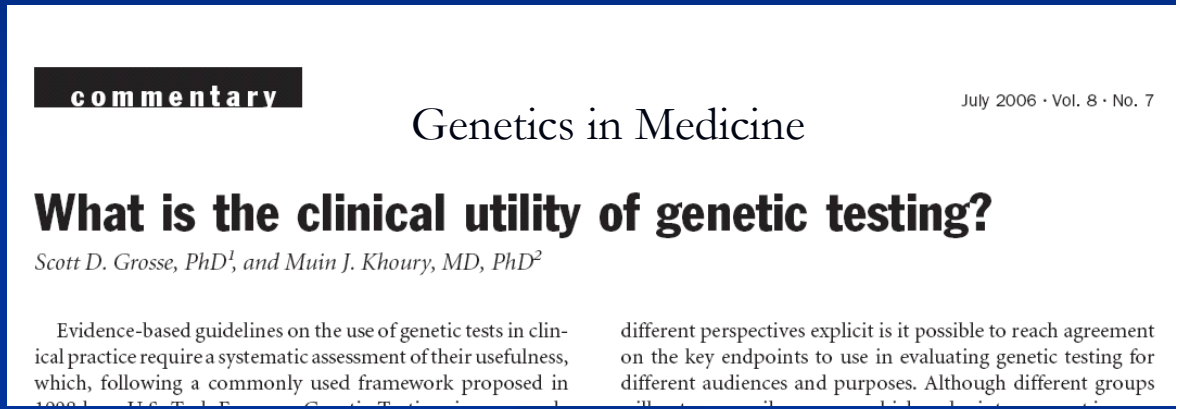


commentary

Genetics in Medicine

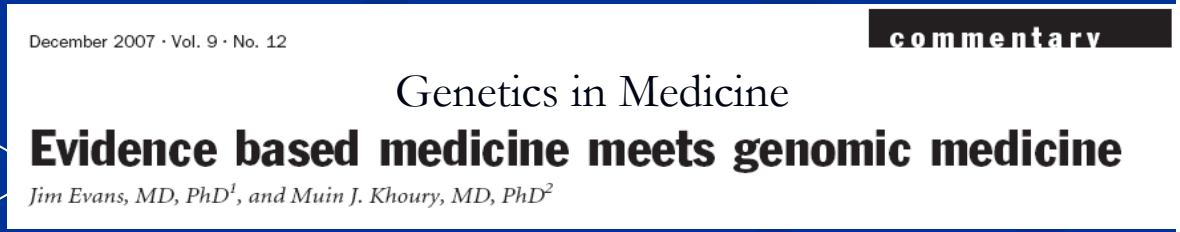
July 2006 · Vol. 8 · No. 7

What is the clinical utility of genetic testing?

Scott D. Grosse, PhD[1], and Muin J. Khoury, MD, PhD[2]

Evidence-based guidelines on the use of genetic tests in clinical practice require a systematic assessment of their usefulness, which, following a commonly used framework proposed in

different perspectives explicit is it possible to reach agreement on the key endpoints to use in evaluating genetic testing for different audiences and purposes. Although different groups



December 2007 · Vol. 9 · No. 12

commentary

Genetics in Medicine

Evidence based medicine meets genomic medicine

Jim Evans, MD, PhD[1], and Muin J. Khoury, MD, PhD[2]

"Clinical utility is in the eye of the beholder"
Anonymous Industry Representative

Case Study 1: Prostate Cancer Susceptibility Testing

- 48 year old white male in good health,
  - father diagnosed with localized prostate cancer at age 68
- Concerned, he got tested using deCODE Prostate Cancer Genetic Test:
  - Relative risk = 1.88
- High risk prompted early PSA test by primary care
  - PSA – high normal at 2.0ng/ml
- High risk prompted urologist to perform TRUS-guided biopsy
  - Positive -Gleason score of 6
  - Radical prostatectomy with nerve sparing

Case Study 2: Dr Oz

- "Dr. Oz found out he's 30 percent less likely than the average man is of developing prostate cancer. Which means, he can be a little less diligent about scheduling regular prostate examinations. "Think of the trade-off," he says. "Thanks to this test, I don't have to have rectal exams

Loci Associated with Prostate Cancer, 2008

Region	p-value	Risk Allele Freq.	Odds ratios	
			Heterozygotes	Homozygotes
8q24 (loc1)	$6.7\ 10^{-16}$	0.1	1.49 (1.34-1.64)	1.83 (1.32-2.53)
10q11	$8.7\ 10^{-14}$	0.38	1.20 (1.10-1.31)	1.61 (1.42-1.81)
8q24 (loc2)	$4.7\ 10^{-13}$	0.50	1.13 (1.02-1.26)	1.46 (1.30-1.64)
17q21	$1.5\ 10^{-10}$	0.52	1.25 (1.13-1.34)	1.47 (1.31-1.65)
11q13	$4.1\ 10^{-10}$	0.50	1.18 (1.08-1.28)	1.48 (1.27-1.74)
10q26	$1.7\ 10^{-7}$	0.25	1.14 (0.94-1.38)	1.40 (1.16-1.69)
7p15	$3.2\ 10^{-7}$	0.76	1.18 (1.07-1.31)	1.54 (1.37-1.73)

NCI CGEMS data, courtesy N Chatterjee, November 2008

So What is Going on Here?

- What do these odds ratios mean? Are they reliable?(clinical validity)
- Are these numbers actionable? What do you do with this information? (clinical utility)
- What would you tell individuals contemplating such testing?
- And what would you tell those already tested?
- Imagine this scenario repeated over multiple diseases in clinical practice? What is the net balance of benefits and harms to the population? to the healthcare system?

The Debate About Prostate Cancer Screening

ORIGINAL ARTICLE

Published at www.nejm.org March 18, 2009
(10.1056/NEJMoa0810696)

Mortality Results from a Randomized Prostate-Cancer Screening Trial

Gerald L. Andriole, M.D., Robert L. Grubb, III, M.D., Saundra S. Buys, M.D., David Chia, Ph.D., Timothy R. Church, Ph.D., Mona N. Fouad, M.D., Edward P. Gelmann, M.D., Paul A. Kvale, M.D., Douglas J. Reding, M.D., Joel L. Weissfeld, M.D., Lance A. Yokochi, M.D., E. David Crawford, M.D., Barbara O'Brien, M.P.H., Jonathan D. Clapp, B.S., Joshua M. Rathmell, M.S., Thomas L. Riley, B.S., Richard B. Hayes, Ph.D., Barnett S. Kramer, M.D., Grant Izmirlian, Ph.D., Anthony B. Miller, M.B., Paul F. Pinsky, Ph.D., Philip C. Prorok, Ph.D., John K. Gohagan,

ORIGINAL ARTICLE

Published at www.nejm.org March 18, 2009
(10.1056/NEJMoa0810084)

Screening and Prostate-Cancer Mortality in a Randomized European Study

Fritz H. Schröder, M.D., Jonas Hugosson, M.D., Monique J. Roobol, Ph.D., Teuvo L.J. Tammela, M.D., Stefano Ciatto, M.D., Vera Nelen, M.D., Maciej Kwiatkowski, M.D., Marcos Lujan, M.D., Hans Lilja, M.D., Marco Zappa, Ph.D., Louis J. Denis, M.D., Franz Recker, M.D., Antonio Berenguer, M.D., Liisa Määttänen, Ph.D., Chris H. Bangma, Bert G.

EDITORIAL

Published at www.nejm.org March 18, 2009
(10.1056/NEJMe0901166)

Screening for Prostate Cancer — The Controversy That Refuses to Die

Michael J. Barry, M.D.

Editor's note: Do the benefits of PSA screening outweigh the risks? Watch video of a roundtable discussion, participate in a poll, and contribute your comments in our Clinical Directions feature — Screening for Prostate Cancer. Commenting closes April 1, 2009.

What is the Evidence of Clinical Utility of Personal Genomics?

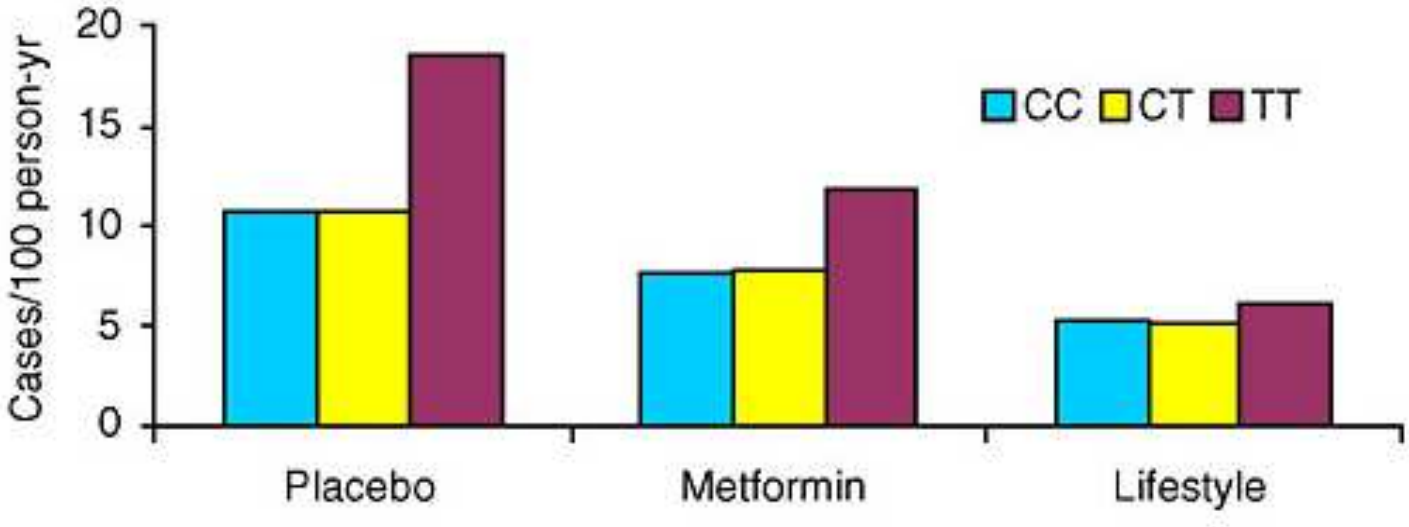


FIGURE 3-4 TCF7L2 and risk of T2D in Diabetes Prevention Program.

SOURCE: Data derived from Florez et al., 2006.

Data from Diabetes Prevention Program (DPP)

RCT results stratified by genotype

”Biomedical Risk Assessment as an Aid for Smoking Cessation?”

- A strategy for increasing smoking cessation rates could be to provide smokers with feedback on the biomedical or potential future effects of smoking,
- Risk assessment includes measurement of exhaled carbon monoxide (CO), lung function, and genetic susceptibility to lung cancer.
- Review of 8 clinical trials

- “Due to the scarcity of evidence of sufficient quality, we can make no definitive statements about the effectiveness of biomedical risk assessment as an aid for smoking cessation”

- Bize et al. Cochrane Review 2008

Outline

- Personal genomics 2009
- A scientific foundation for personal genomics
- Recommendations of NIH-CDC workshop December 2008

Putting Science over Supposition in the Arena of Personal Genomics NIH-CDC Multidisciplinary Workshop

National Cancer Institute
U.S. National Institutes of Health | www.cancer.gov

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Public Health Genomics
Cancer.gov en español

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1-800-4-CANCER

Personal Genomics Workshop
December 17-18, 2008
Bethesda North Marriott, Bethesda, Maryland

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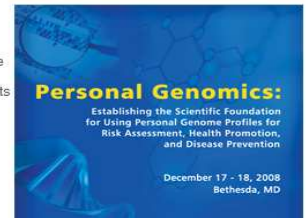
Purpose

This 2-day workshop, cosponsored by CDC and NIH, explored the type of scientific foundation that is crucially needed to make the promise of personal genomics a reality. The workshop participants examined how the integration of genomics into personalized health can follow an evidence-based process. The process for using genomic applications in personalized healthcare (e.g. pharmacogenomics, early detection markers, testing in clinical trials) was discussed.



A multidisciplinary working group reviewed and discussed the

The scientific foundation for personal genomics: recommendations from an National Institutes of Health–Centers for Disease Control and Prevention Multidisciplinary Workshop

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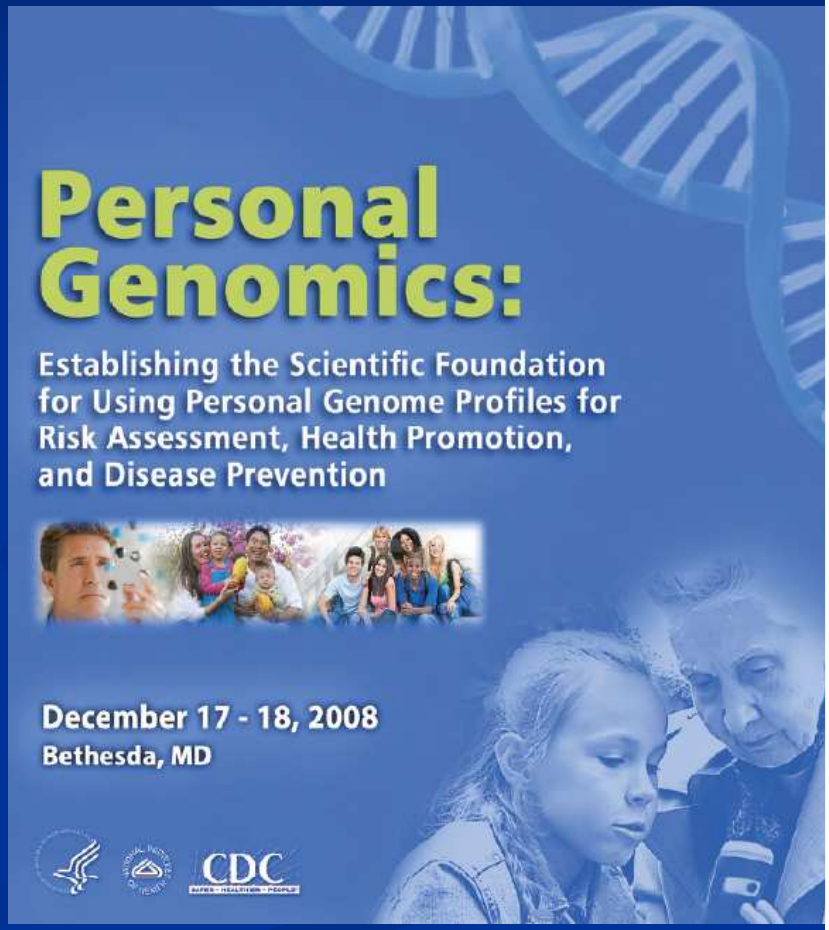

Genetics in Medicine Aug 2009

Personal Genomics: Workshop Recommendations

- Develop and implement industry-wide scientific standards for personal genomics

Personal Genomics: Workshop Recommendations

- Develop and implement industry-wide scientific standards for personal genomics

- Develop and implement a multidisciplinary research agenda

Personal Genomics: Workshop Recommendations

Table 3 Multidisciplinary research needed for evaluating personal genomics to improve health and prevent disease

Field	Scientific research	Current issues
Epidemiology	Genotype prevalence, calculating risks associated with genetic variants, gene–gene, and gene environment interactions	Data currently lacking on magnitudes of risks especially for joint effects of genes and environment
Clinical evaluation	Quantify added value of personal genomics in reclassifying risks compared traditional risk factors	Data currently suggest weak discriminatory ability of personal genomics compared with other factors. It is not yet clear what are the net health benefits versus harms in using personal genomics in prevention and clinical care
Behavioral and social sciences	Assess how genome profiles affect behavior of individuals, families and populations	Data from other fields suggest that behavior change is difficult. It is not clear if genome information matters
Communication sciences	Study communication and education strategies for using genomic information to improve health	Provider and consumers are not equipped to deal with this type of information
Health services research & Public health surveillance	Assess impact of genome info health outcomes in the real world, health disparities, and economic indicators	Expensive technology when applied in populations; unknown health benefits and potential harms

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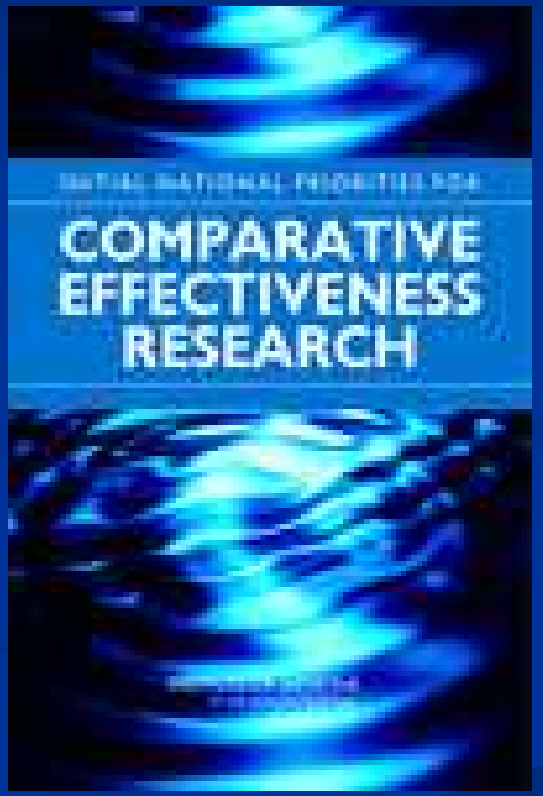
Comparative Effectiveness Research and Genomic Medicine (IOM Priorities)

- "Compare the effectiveness of adding information about new biomarkers (including genetic information) with standard care in motivating behavior change and improving clinical outcomes"

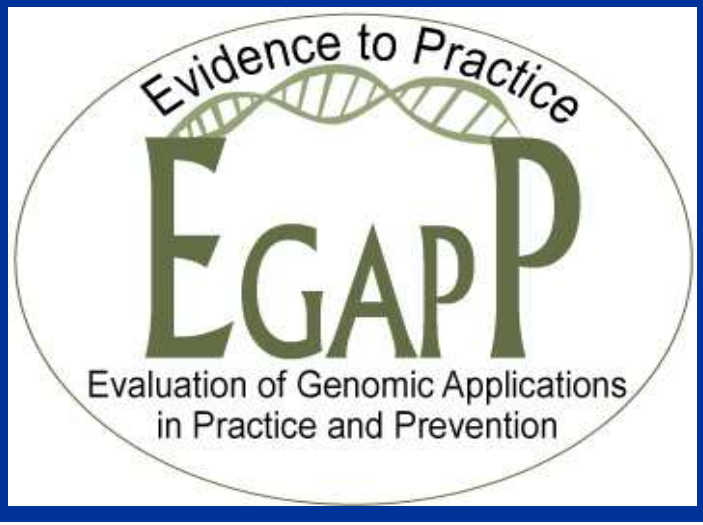


Personal Genomics: Workshop Recommendations

- Develop and implement industry-wide scientific standards for personal genomics
- Develop and implement a multidisciplinary research agenda
- Enhance credible knowledge synthesis and dissemination of information to providers and consumers
- Link scientific research on validity and utility to evidence-based recommendations for use of personal genomic tests

EGAPP Initiative

Evaluation of
Genomic
Applications in
Practice and
Prevention



- Independent multidisciplinary Working Group
- Evidence-based, transparent, and publicly accountable
- 4 components: horizon scan; systematic reviews; appraisal and recommendations; evaluation of impact

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- Develop and implement a multidisciplinary research agenda
- Enhance credible knowledge synthesis and dissemination of information to providers and consumers
- Link scientific research on validity and utility to evidence-based recommendations for use of personal genomic tests
- Consider the value of personal utility

The Scientific Bottom Line on Personal Genomics in 2009

Genet Med August 2009

COMMENTARY

Personal utility and genomic information: Look before you leap

Scott D. Grosse, PhD[1], Colleen M. McBride, PhD[2], James Evans, MD, PhD[3], and Muin J. Khoury, MD, PhD[4]

In this issue, Foster et al.[1] argue that the utility of personal genomic information and the level of evidence that is required to document utility depend on the context and audience. Similarly, others have suggested that the utility of genomic information be considered from three perspectives: the public health perspective, which emphasizes health improvements on a population level; the clinical perspective, which emphasizes the use of genomic information in diagnostic thinking and therapeutic choice; and the personal perspective, which may consider genomic information as having potential value per se, positive

construct and rigorous assessments of personal utility will be challenging.

Research has shown that most individuals in families affected by Alzheimer disease who were given the opportunity to learn their apoliopoprotein E (APOE) genotype status perceived the results to have personal utility. They felt that it helped them prepare for the future, despite a lack of intervention options, and those tested generally did not experience adverse psychological effects.[5,6] However, genetic testing for Alzheimer disease may be the high water mark for personal utility, as such strong