Personal Genomics:
What Kind of Information Do Primary Care Providers Need? What Is the Role of Evidence-Based Guidelines?

Greg Feero, M.D., Ph.D.
Chief, Genomic Healthcare Branch
National Human Genome Research Institute
National Institutes of Health

Outline

- A primary care perspective on health care and genomics
- Requisites for appropriate use of personal genomic profiles
- Guidelines
- Looking ahead….

The Health of Our Society

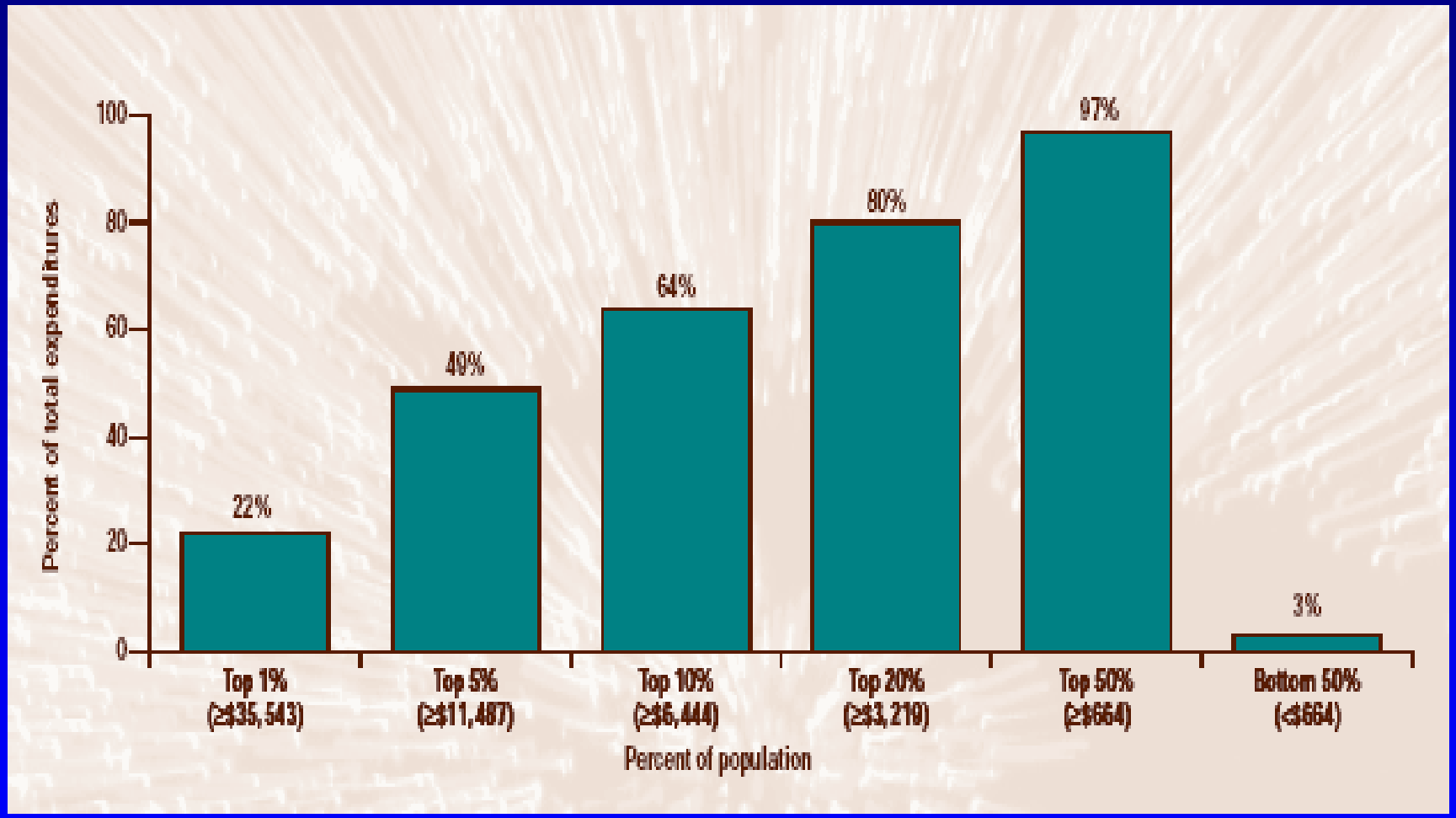
- **$2.26 trillion dollars spent on health care in the U.S. in 2007 (16% GDP)**
- **About equal to the total GDP of France, Italy or the U.K., yet lower life expectancy.**
- **47 million (1 in 7) uninsured**

Common chronic disease is dragging down the system:

- 130 million Americans affected
- 7 of 10 deaths
- $0.75 of every dollar spent on health care
- 2/3 of growth in health care spending in the last 20 years

Almanac of Chronic Disease, 2008 ed.
Partnership to Fight Chronic Disease

Percent of Total Health Care Expenses Incurred by Different Percentiles of U.S. Population: 2002



Source: Conwell LJ, Cohen JW. Characteristics of people with high medical expenses in the U.S. civilian noninstitutionalized population, 2002. *Statistical Brief* #73. March 2005. Agency for Healthcare Research and Quality, Rockville, MD.

Solutions – primary care style…

- **33%** of diabetics are undiagnosed --- blood glucose. **(Almanac, 2008)**
- **24%** of hypertensives undiagnosed --- blood pressure measurements. **(Almanac, 2008)**
- **37%** of high cholesterol undiagnosed --- fasting lipid panel. **(Almanac, 2008)**
- **Universal health care, better screening programs, smoking cessation, exercise programs, improved nutrition etc…**

“We are installing 10,000 ICDs per month in the U.S.”

Harvard Cardiology Professor
6/2008

Return to Previous Page

American Family Physician
PUBLISHED BY THE AMERICAN ACADEMY OF FAMILY PHYSICIANS FEBRUARY 15, 2000

CLINICAL OPINION

Medicine and Society

The Impact of Genetic Testing on Primary Care: Where's the Beef?

ERIC A. WULFSBERG, M.D.
University of Maryland School of Medicine,
Baltimore, Maryland

Over the past decade, there has been a rising cacophony of predictions that genetic discoveries emerging from the Human Genome Project would revolutionize primary medical care. However, despite these predictions, genetic practice in primary care has undergone little change. This paradox is in part due to the exuberance and optimism of the genetic community about genetic testing that has its roots in the early successes of newborn screening and prenatal carrier testing. However, the lack of effective interventions for people with these disorders or who are carriers of genetic diseases and increasing public apprehension about genetic testing will slow down adoption of genetic technologies into primary care medicine. It also appears likely that before widespread genetic testing will be offered, practice guidelines, educational materials for providers and patients, informed-consent protocols and laboratory standards for genetic testing will need to be developed.

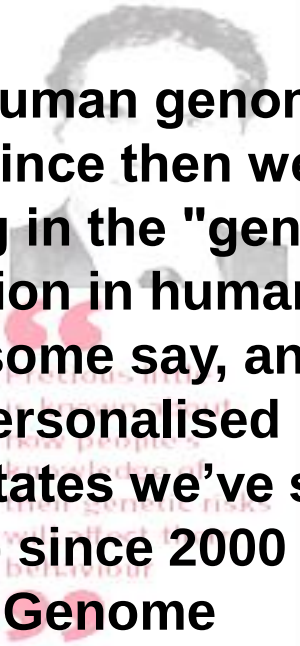
Many review articles and descriptions of programs designed to teach primary care physicians the basics of new genetic technologies have been appearing in medical journals[1] and are accessible online.[2] Twelve years ago, the following millennial prediction appeared in *U.S. News and World Report*:

Most people will be getting genetic profiles by the year 2000, predicts Michael McGinnis, director of the U.S. Office of Disease Prevention and Health Promotion. Health care will improve dramatically, he argues, because knowing one's risks will motivate lifestyle changes far more powerfully than

Douglas Kamerow

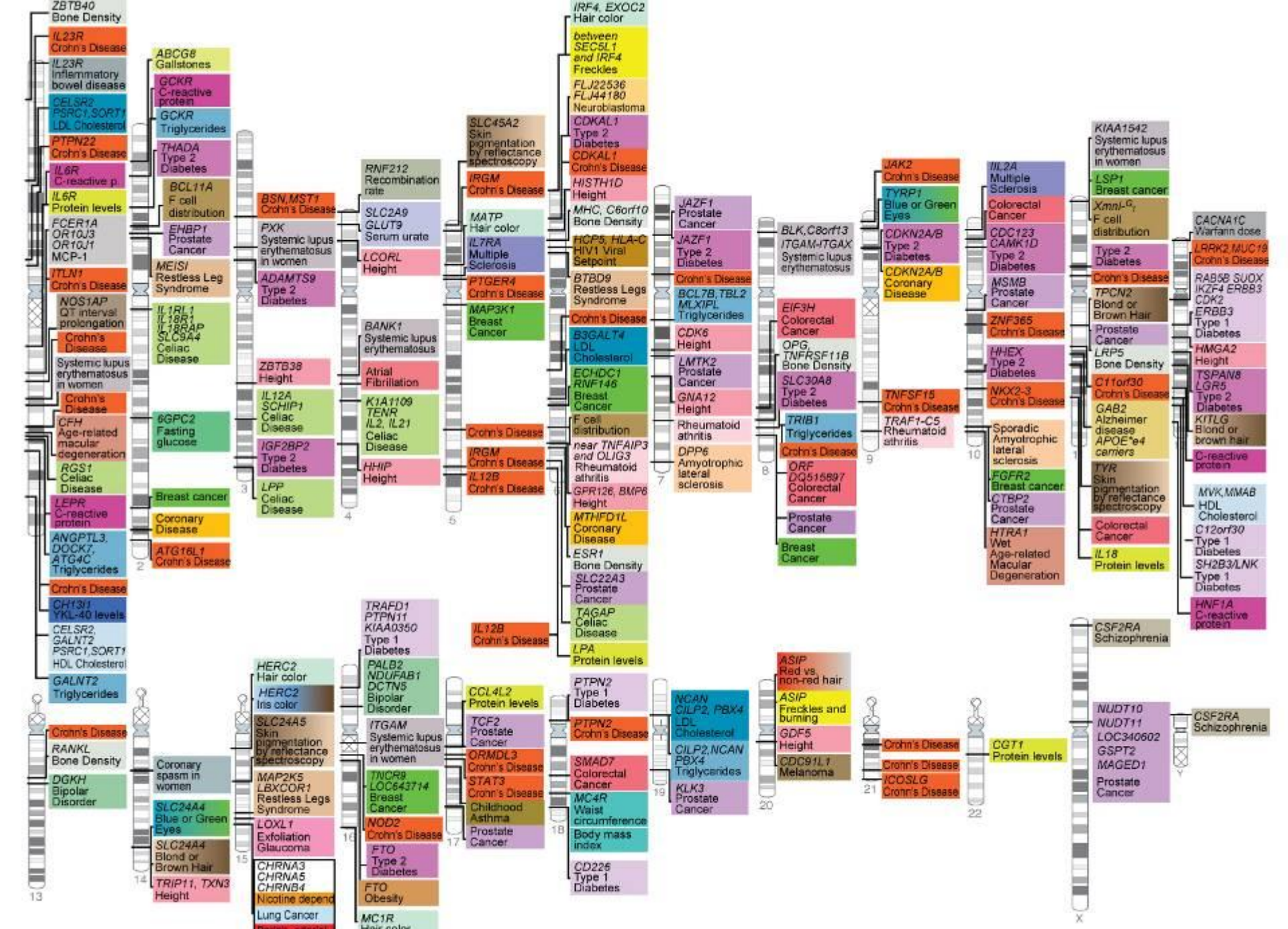
Waiting for the genetic revolution

Will 2008 be the year that genomics delivers on its promises?



“The sequencing of the human genome was completed in 2003. Since then we’ve been told that we’re living in the "genomic era"—the biggest revolution in human health since antibiotics, some say, and the beginning of scientific, personalised medicine. In the United States we’ve spent about $4bn (£2bn; 2.8bn) since 2000 to fund the National Human Genome Research Institute, so it seems fair to ask what we’ve got for our money. “

BMJ 2008;336:22 (5 January)



Manolio, Brooks, Collins, J. Clin. Invest., May 2008

Translating Genomics…

- Genomic discoveries relevant to common disease diagnosis and management are coming at an increasing rate.
- Basic discoveries are leading to the development of clinical applications.
- Ergo, improved healthcare is around the corner!


Analytic Validity?
Clinical Validity?
Harms?
Disparities?
Education?
Intellectual property?
Clinical Utility?
Benefits?
Informed consent?

Translating Genomics…

- **Genomic discoveries relevant to common disease diagnosis and management are coming at an increasing rate.**
- **Basic discoveries are leading to the development of clinical applications.**

Mind the gap!

- **Ergo, improved healthcare is around the corner!**

The current system favors largely unfiltered access of new testing technologies to the health care market.

Downstream consequences???

…ask your health care provider.

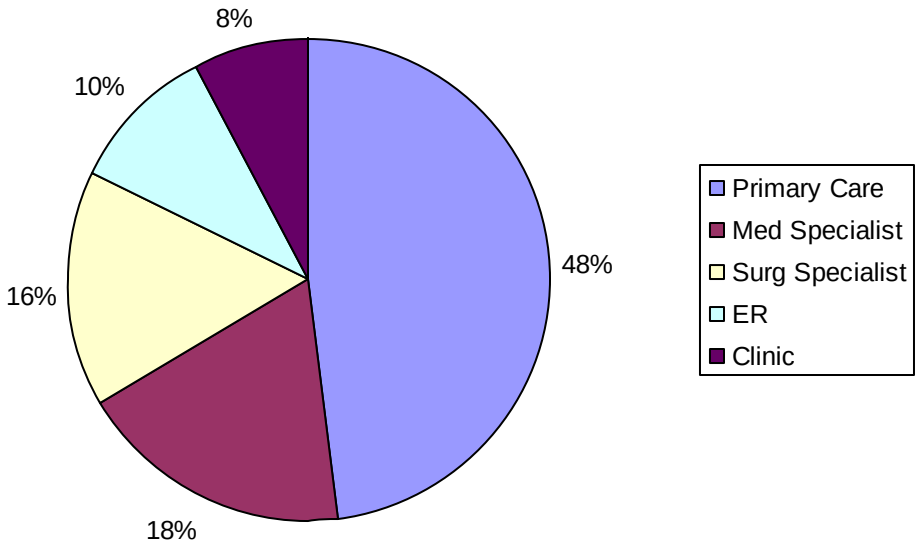
Assumption:

As our care delivery system is currently framed, appropriate integration of multiplexed predictive genetic tests into healthcare requires clinicians to have a fair knowledge of genomics and statistics.

Knowledge: Genomics

1.1 Billion Ambulatory Visits in 2004 in the U.S.

CDC data



Primary Care

"If you knew there was a genetic disorder already present in your immediate family, with what or whom would you be most likely to consult to learn about the possibility of inheriting it?"

- 71% chose their PCP

1998 AMA survey of 1000 U.S. Adults

MD geneticists represent 0.18% of the 700,000 physicians in the U.S.

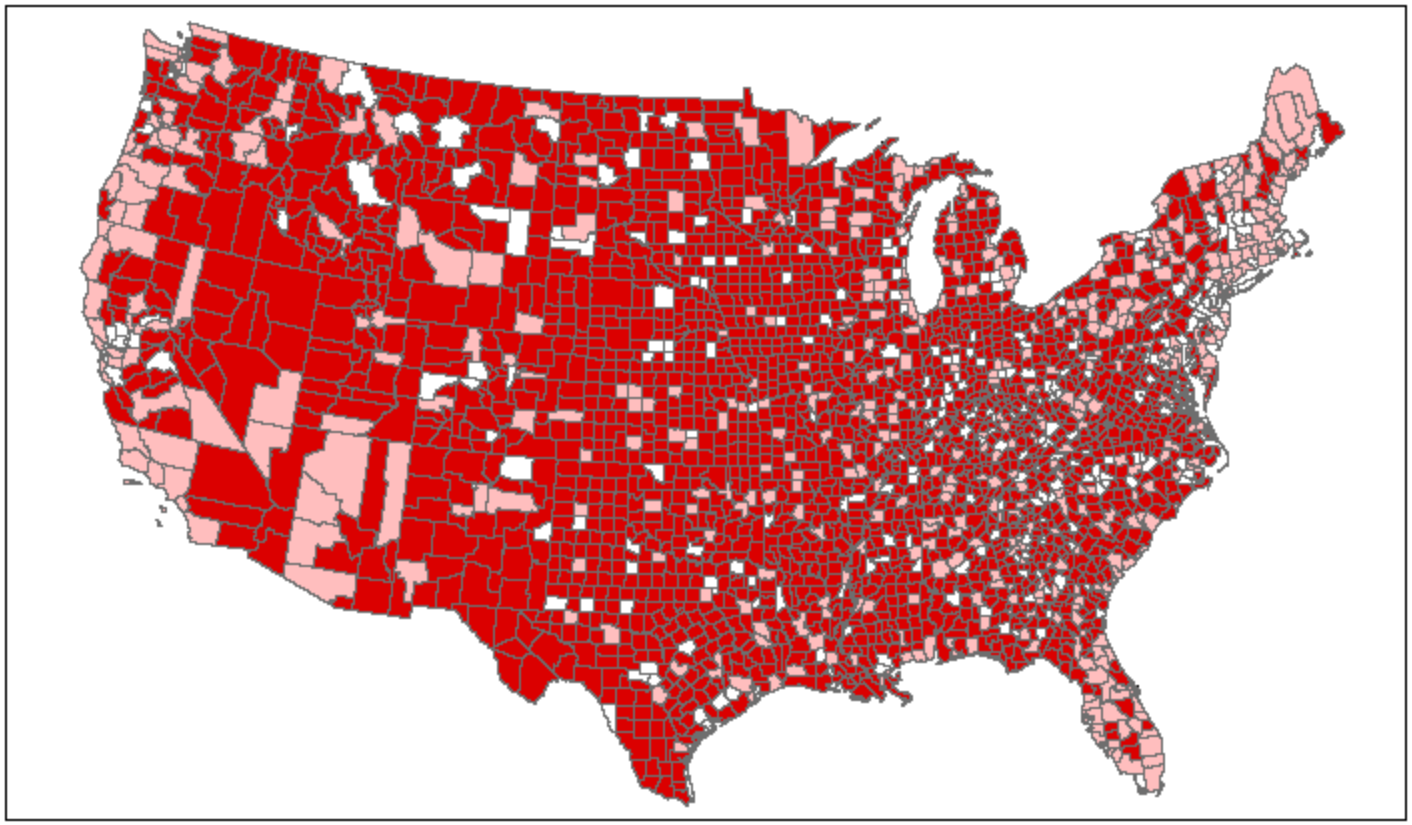
ACMG testimony before SACGHS, Nov. 2007

Genetic counselors:

NSGC web site and places I've lived + 50 miles:

	2006	2007
Pittsburgh, PA –	8	14
Vienna, VA –	40	60
State College, PA –	0	0
Durham, NC –	18	28
Waterville, ME –	0	0

PRIMARY CARE HEALTH PROFESSIONAL SHORTAGE AREAS
IF FAMILY PHYSICIANS WERE WITHDRAWN



2002 County Primary Care
HPSA Status After Withdrawal

- HPSA/Becomes Full HPSA
- Remains Partial HPSA
- Not a HPSA

www.graham-center.org

Prepared by the Robert Graham Center: Policy Studies in Family Medicine and Primary Care

Data Source: 2003 Area Resource File (U.S. Department of Health and Human Services)

Education

- Genetics community has been reaching out for years with varying degrees of success
  - Genetics in Primary Care
  - Genetests/Geneclinics
  - MOD education modules
  - NEJM Genetics articles
  - NCHPEG
  - Meeting presentations

Table 2
Provider types and knowledge scores

Provider type	No. to consult provider Type *N* (% of 5915)	Respondents' ratings of providers' knowledge of the genetics of the condition in their family		
		Poor	Average	Good or excellent
Family practice/primary care	3179 (53.7%)	39%	27%	34%
Pediatrician	2530 (42.7%)	27%	25.3%	47%
Cardiologist/electrophysiologist	2062 (35%)	22%	22%	56%
Neurologist	1885 (31.8%)	21%	23%	56%
Ophthalmologist/retinal specialist	2060 (34.8%)	22.6%	22.4%	55%
Pulmonologist	923 (15.6%)	20.2%	21%	58.8%
Endo				
Hema				
Derm				
Gastr				
Surge				
Psych				
Ortho				
Gynec				
Neph				
Speech-language pathologist	1546 (26%)	32.7%	25.4%	41.9%
Rheumatologist	341 (5.8%)	38.6%	20.2%	41.2%
Nutritionist	1191 (20%)	36.8%	24.1%	39.1%
Otolaryngologist	869 (14.6%)	29.5%	24.9%	45.7%
Physical therapist	1949 (33%)	31.4%	24.8%	43.8%
Urologist	693 (11.7%)	34%	20.9%	45.1%
Occupational therapist	1726 (29%)	31.2%	26.6%	42.2%
Allergist/immunologist	815 (13.8%)	52.1%	22.5%	25.4%
Social worker	965 (16%)	42.8%	24.7%	32.5%
Emergency physician	1100 (18.6%)	62%	20.6%	17.4%

The 25 provider types listed here represent 95% of all providers identified by respondents in the management of their condition.

Table 2 Provider types and knowledge scores
From: Harvey: Genet Med, Volume 9(5):May 2007.259-267

Over 50% of IM/FP/Peds/OBGyns rated as having a poor or average knowledge of genetics of conditions in their family….

Harvey et al., Genet Med. May 07

Knowledge: Statistics

Statistics/risk communication:

- Internal medicine residents and statistics (277 in 11 programs)
  - 95% acknowledged statistics important
  - 75% acknowledged that they didn't fully understand statistics in the literature
  - Scored 41% on an exam designed to test statistics understanding
  - Faculty scored 72%

Windish et al., JAMA Sept. 2007

Statistics/risk communication:

- Med students, internal medicine residents and faculty and statistics (301 at Mayo)
  - 93% acknowledged statistics important to EBM
  - 18% felt statistics training was sufficient
  - 23% reported that they could identify the correct use of statistics in a study.

West and Ficalora, Mayo Clin Proc., 2007

Statistics/risk communication:

- Risk communication to patients by family physicians (300 providers in Massachusetts)
  - 93% agreed qualitative risk communication was important, 87% were confident that they could do so.
  - 76% felt quantitative risk communication was important, **36%** were confident that they could do so.
  - **One in ten** considered themselves ineffective in communicating risk!

Lies, damn lies, and statistics:

- Concepts like relative risk and odds ratios are slippery, and have been used, on occasion, to impress rather than inform the uninitiated.

- In EBM world concepts like **absolute risk**, **positive/negative predictive power** and **numbers needed to treat (test)** are much better representations of ‘truth’.

Primary care providers are not well prepared to make rational decisions regarding the current round of genetic tests for common complex conditions.

Except perhaps to ignore the issue…

Clinical guidelines:

- Widely accepted as a way to standardize and improve practice
- Serve as a basis for P4P programs
- Numerous (perhaps too many) organizations promulgate guidelines
- In U.S. largely elective*, in other developed nations may be mandatory

* The legal system acts largely as an enforcer

Clinical guidelines:

- All guidelines are not created – or viewed-equally
  - Level of evidence (USPSTF vs. specialty societies)
  - Country of origin
  - Organization of origin
- Guidelines have, on occasion, been used to promote opinion rather than fact.

"We identified only 1 RCT of a genetic testing intervention for a common condition that measured a clinical outcome."

- Scheuner et al., JAMA 2008

Clinical guidelines:

- Adherence to guidelines with an excellent evidentiary base remains sub-optimal
  - Secondary risk reduction for ACS is an excellent example
- Knowledge of guidelines is necessary but not sufficient (access to downstream services, adherence, time to counsel, tools for education etc)

Guidelines continued:

Attitudes of primary care providers toward clinical practice guidelines – meta-analysis of 17 qualitative studies from U.S. and Europe.

Carlsen et al., British Journal of General Practice, Sept. 2007

Guidelines continued:

1. Guideline quality and applicability
2. Personal experience
3. Doctor-patient relationships - rationing
4. Professional responsibility – risk avoidance
5. Practical issues - time to access and negotiate
6. Guideline format – keep it simple

Technology
PUBLISHED BY MIT Review

Monday, October 06, 2008

Five Thousand Bucks for Your Genome

A new sequencing service could change the face of human genomics.

By Emily Singer

Starting next spring, a complete human-genome sequence can be ordered for just $5,000, thanks to a new sequencing service announced by Complete Genomics (http://completegenomics.com/index.html) , a startup based in Mountain View, CA. The stunning price drop--sequencing currently costs approximately 20 times that amount--could completely change the way that human-genomics research is done and open up new possibilities in personalized medicine. Researchers say that a $5,000 genome would enable new studies to identify rare genetic variants linked to common diseases, and it could open up the sequencing market to diagnostic and pharmaceutical

““….gizmo idolatry refers to the general implicit conviction that a more technological approach is intrinsically better than one that is less technological… Many gizmos make so much sense, in the absence of evidence or even the presence of evidence to the contrary, that their value or utility is persuasive prima facie.”

Leff and Finucane, “Gizmo Idolatry”
- JAMA, April 16, 2008

"PCPs were nearly unanimous in the belief that information about the 'clinical relevance' of testing – i.e. whether interventions are available to modify risk or to treat a diagnosed condition – would be an essential component of any educational resource."

Trinidad et al. Community Genet 2008;11:160–165

"The bulk of this {healthcare} spending growth, however, appears to result not from increasing disease prevalence but from the development and diffusion of new medical technologies and therapies."

Orszag PR, Ellis P. NEJM Nov. 1 2007

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THE OFFICE OF THE PRESIDENT-ELECT

"Today we begin in earnest the work of making sure that the world we leave our children is just a little bit better than the one we inhabit today."
President-elect Barack Obama

NEWSROOM: BLOG

Analysts praise choice of Orszag and Nabors

Tuesday, November 25, 2008 05:37pm EST / Posted by Dave Rochelson

Following President-elect Barack Obama's announcement today of two more members of his economic team, analysts and congressional leaders from both sides of the aisle are calling the selections "excellent."

The Washington Post calls Peter Orszag, Director-designate of the White House Office of Management and Budget (OMB), "widely respected for his work on how Americans receive medical care... Orszag has carved out a niche as a leading international thinker on health policy."

Rep. Paul Ryan (R-WI) applauded the choice of Orszag. "He has proven his mettle as one of our nation's leading expers on the federal budget," Ryan was quoted as saying in MSNBC's First Read. "He and I have enjoyed a strong, productive working relationship, and I have been particularly impressed with his understanding of the looming entitlement crisis, and the critical need for action."

UPCOMING EVENTS

THE INAUGURATION
JANUARY 20, 2009 *in* WASHINGTON, DC

THE AGENDA

- Revitalizing the Economy
- Ending the War in Iraq
- Providing Health Care for All
- Protecting America
- Renewing American Global Leadership

Conclusions

- PCPs are “relentlessly practical”
- PCPs are vulnerable to “asymmetric knowledge”
- Guidelines based on health outcomes are critical, but are not enough
- Utility is very important to PCPs and value should be important to all of us….