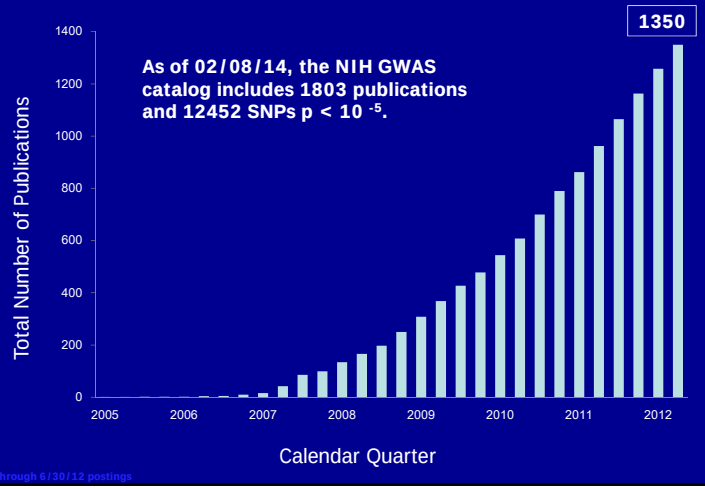
The Scientific Value of Incorporating Genomics into NHANES

Sharon L.R. Kardia, Ph.D
University of Michigan
February 2014

Genomics Today

- Bares little resemblance to what we've done before 2007
- Is a large collaborative effort
- Needs large sample sizes
- Individual level data is shared via dbGAP
- Has a different set of 'rules' on sample sizes, analysis, replication
- Would benefit greatly from having NHANES

Published GWA Reports, 2005 – 6/2012



GWAS opportunities multiply like rabbits and then evolve to next species

2008 2009 2010 2011 2012 2013 2014

First GWAS projects

Consortiums form: CHARGE, GIANT, MAGIC, CARE, SHARE, GENEVA, ICBP ...

dbGAP begins

HapMap imputation of 2.5 mill SNPs

Hundreds of GWAS published on every conceivable organ, biomarker, and characteristic:

- Heart, Kidney, Brain, Eye...
- Glucose, Lipids, CRP...
- BP, BMI, Height, Weight...
- Age of menopause, menarche, reproduction, first sex...
- Optimism, well being, conscientiousness, education...
- Longevity, gait, grip strength...

Shift to 1000 Genomes Project imputation to 25 million SNPs

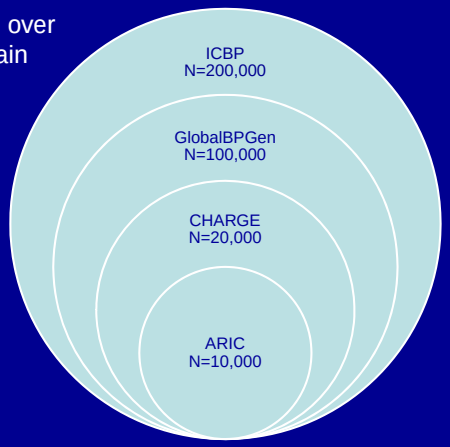
Exome Chip

Exome Sequencing

Whole Genome Sequencing

The Russian Doll movement in GWAS

Data is used over and over again



Genomics is still expanding

Collaborators (conference calls)	Sample Size (Discovery + Replication)	# Mutations (SNPs, CNVs, rare mutations)
3	500	10,000
6	1,000	50,000
9	5,000	100,000
27	10,000	500,000
81	50,000	1,000,000
243	100,000	2,500,000
729	500,000	5,000,000
	1,000,000	Complete sequence

NHANES has a wealth of areas

- Cardiovascular disease
- Diabetes
- Bone status, osteoporosis
- Oral health
- Vision and eye diseases
- Hearing and balance
- Fitness and strength
- Reproductive health

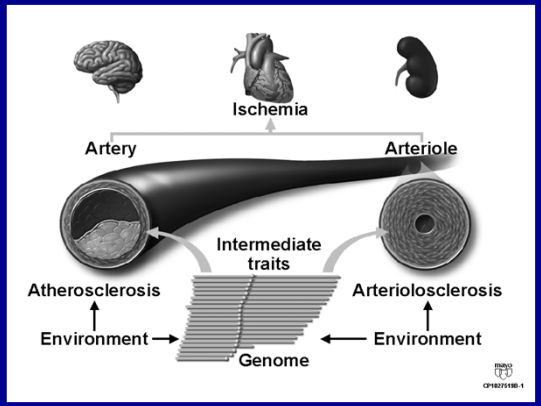
NHANES has key data in tough arenas for genomics

- Nutrition
- Mental health
- Risk behaviors
- Allergies
- Environmental exposures
- Infectious diseases

Sifting through the tough options

- Option 1: Don't measure genomes at all
  - Would waste a national treasure's ability to accelerate knowledge...
  - Could significantly delay gene-environment studies...
  - Delays our ability to understand the distribution of rare functional mutations...
  - Could delay new genomic discoveries integrating infectious, chronic, and environmental health outcomes...

Looking across many traits we're more likely to understand more about the biology



Summary of 'Functional' Variants for Key Genes in HRS Study

Gene	Number of SNPs from 1000G (Info>0.8)	Number of functional SNPs	Number of SNPs from Exome chip	Number of functional SNPs from Exome chip
APC	920	5	51	47
BRCA1	352	12	53	50
BRCA2	414	22	96	90
CFTR	1003	10	79	76
HbB	82	0	9	9
LDLR	379	3	40	19
PAH	903	3	16	16

* 'Functional' variants include missense, nonsense, and splice-site

Number of 'functional' SNPs by Minor Allele Frequency in HRS

	1000G MAF<0.001	1000G 0.001<MAF<0.05	1000G 0.05<MAF
APC	0	4	1
BRCA1	1	5	7
BRCA2	1	19	2
CFTR	1	8	1
HbB	0	0	0
LDLR	0	2	1
PAH	0	3	0

Number of 'functional' SNPs by Minor Allele Frequency in HRS

	Exome Chip MAF<0.001	Exome Chip 0.001<MAF<0.05	Exome Chip 0.05<MAF
APC	37	9	1
BRCA1	37	7	6
BRCA2	55	34	1
CFTR	58	17	1
HbB	7	2	0
LDLR	17	1	1
PAH	14	2	0

The rare 'functional' variants are often the most important to people and geneticists

Sifting through the tough options

- Option 2: Measure genomes and do not report
  - Right now we do not have enough replicated findings to report Pr(disease | genotype) on most variants. NHANES could help develop this knowledge base.
- Option 3: Measure genomes and report 'Bin 1'
  - A potentially frustrating option where participants might be able to know their results BUT researchers could NOT study/report because it violates confidentialty policy

The big stumbling block

The sharing of individual-level genetic data to researchers is prohibited.

The wonderful aspects of having NHANES will be limited for the 'functional' variants researchers are most interested in studying

If we can't share them widely, why measure them?

Key contributions of NHANES

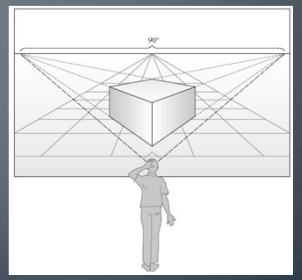
- Large sample size of high quality measures
- Unparalleled environmental measures
- Ability to integrate across a wide range of traits
- Large sample size is essential for examining rarer variants

What data are returnable?

Marc S. Williams, MD
Director, Genomic Medicine Institute
Geisinger Health System

Objectives

- Define types of results
- Consider return from different perspectives
- Aspects of clinical vs. research return



Type of Results

- Actionable variants
  - Occur in genes with known clinical effect
  - Different types
    - "Deterministic" (*BRCA1*)
    - Predisposing (C282Y in *HFE*)
    - Carrier status (*CFTR*)
    - Pharmacogenomic (*CYP2C19*)

Type of Results

- Non-actionable variants
  - In genes associated with clinical condition but no treatment of change in care is available (ApoE4, Huntington expansion)
- Variants of uncertain significance (VOUS)
  - Occur in genes associated with clinical condition but the effect of the variant is unknown (most missense variants in *BRCA1*)
- The rest of the genome

Perspectives-Clinician (Systems?)

- Actionable variants-Yes but…
  - Primary vs. incidental
  - Clinical context
  - Level of evidence
- Non-actionable variants-No
  - Creates concern in patient with no benefit
  - Will increase health care costs
- VOUS and the rest-Get back to me when you know something useful

Perspectives-Patient (GHS)

- Actionable variants-Yes
  - Primary and incidental
  - Will use this for myself and family members
- Non-actionable variants-Yes
  - Important to know
  - May still use for healthy lifestyle changes (ApoE4)
- VOUS and the rest-Yes
  - We know you're busy and we'll help you to manage the new knowledge
- Similar to other published reports (Wright et al. Genet Med 2014)

Perspectives-Government

- Not concerned with types of variants, but with role of clinician in return
- **BREAKING NEWS!!** HHS (CMS, CDC, OCR) 2/3/14
  - Amendment to the Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations
    - Allows laboratories to give a patient access to the patient's completed test reports on the patient's … request.
  - Eliminates the exception under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule to an individual's right to access his or her protected health information when it is held by a CLIA-certified or CLIA-exempt laboratory.

Perspectives-Government

"The right to access personal health information is a cornerstone of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. Information like lab results can empower patients to track their health progress, make decisions with their health care professionals, and adhere to important treatment plans."

- Secretary Kathleen Sebelius

Perspectives-Government

- Questions
  - Does this apply to research or only clinical tests?
  - Does this apply to research results generated by a CLIA-certified laboratory?
  - How does this relate to the Presidential Commission report?

Perspectives-Researchers

- Variable
- Depends on study?
  - Anonymized study
    - Do highly actionable variants warrant breaking anonymization for return?
  - Are participants consented for return of results?
    - Can (should) highly actionable results be returned even if not consented for return?
  - Is the purpose of the study to examine the question of return of results?
    - What if a participant with a highly actionable result is randomized to the non-return group? (Wisconsin CF newborn screening)

Perspectives-Researchers

- Burke et al. Return of Results: Research Versus Clinical Care Am J Med Genet (in press)
- Organizing Question: "If clinical relevance is the motivation for returning research results, how does this process differ from returning test results in clinical care?"

Research vs. Clinical Care

Clinical Care

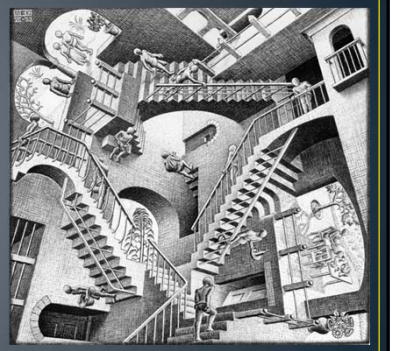
- Optimizing health care of individuals
- Provide care in best interest of patient
- Patient has the right to access all clinical information
- Treatment takes place in context of provider-patient relationship

Research

- Production of generalizable knowledge
- Protect participant from harm
- Preserve integrity of study
- Avoid the 'therapeutic misconception'
- No consensus or legal requirement that participants have access to information
- Provider patient relationship is not created through participation in research study

Conclusion

- What research data are returnable?
- It depends on your perspective



What NHANES Genomic data are returnable?

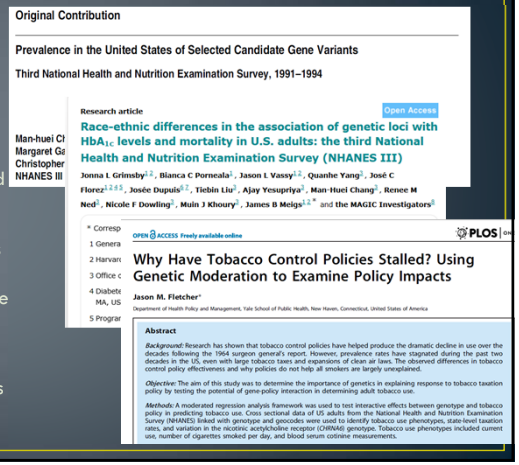
Muin J. Khoury MD, PhD
Director, Office of Public Health Genomics
Centers for Disease Control and Prevention

CDC NHANES Public Health Genomics Work

- 1994 Workshop
- 1997 OPHG
- 2003: Candidate Genes
- 2008: GWAS (Beyond Gene Discovery Initiative)
- 2011: Workshop-binning
- 2014: Here we are
- Future: Sequencing
- Other genome-based markers

Public Health Utility of NHANES Genomics Data: Beyond Gene Discovery

- Prevalence of genomic variants
- Genes and health status
- Gene-environment interactions (stratified analyses)
- Genetic testing issues
- Unique representative US population health survey
- But comes with strings attached


Original Contribution

Prevalence in the United States of Selected Candidate Gene Variants

Third National Health and Nutrition Examination Survey, 1991–1994

Research article — Open Access

Race-ethnic differences in the association of genetic loci with HbA_{1c} levels and mortality in U.S. adults: the third National Health and Nutrition Examination Survey (NHANES III)

Why Have Tobacco Control Policies Stalled? Using Genetic Moderation to Examine Policy Impacts

Jason M. Fletcher

Issues to Consider for Genomic RORs in NHANES

- **Nature of the Survey**: Govt statistical survey- cross section of population (not clinical practice-not typical research but public health practice)
- **Nature of Informed consent** process (can be changed for future NHANES)
- **Utility limited** because of access & ability to do genetic analysis (Data Enclave Model)
- **Is genetic information different** from other info collected in NHANES?
- **Evidentiary basis for ROR** (clinical validity or clinical utility, ACMG, EGAPP, NHGRI)
- **Issue of "opportunistic" screening**

DHHS3

Evaluation of Genomic Applications in Practice and Prevention Initiative (EGAPP)

- A unique experiment
- Independent, multidisciplinary panel since 2005
- Systematic, evidence-based process to assess validity & utility of genomic tests & family health history
- New methods for evidence synthesis and modeling in 2013, including next generation sequencing and stratified screening
- 10 recommendation statements to date
  - Colorectal cancer, breast cancer, heart disease, clotting disorders, depression, diabetes, prostate cancer
- Uncovering major knowledge gaps and setting a translational research agenda
- Can it be adapted to NHANES?

Healthy People 2020

EGAPP Framework

- Specific Information for Each Clinical Scenario using ACCE Framework
- Four components
  - Analytic Validity (AV): Lab performance
  - Clinical Validity (CV): Genotype-phenotype correlation
  - Clinical Utility (CU): Improved health outcomes
  - ELSI

Genetics IN Medicine • Volume 13, Number 6, June 2011

COMMENTARY

Deploying whole genome sequencing in clinical practice and public health: Meeting the challenge one bin at a time

Jonathan S. Berg, MD, PhD[1], Muin J. Khoury, MD, PhD[2], and James P. Evans, MD, PhD[1]

- Current practices in medical genetics may not be suitable for genome-wide analysis
- Need for evidence-based, structured computational analysis for diagnostic and incidental results

"Binning" Framework

	Criteria:	*Clinical Utility*	*Clinical Validity*			*Unknown Clinical Implications*
Genes	Bins:	**Bin 1 Medically actionable incidental information**	**Bin 2A Low risk incidental information**	**Bin 2B Medium risk incidental information**	**Bin 2C High risk incidental information**	**Bin 3 All other loci**
	Examples:	*BRCA1/2 MLH1, MSH2 FBN1 NF1*	PGx variants and common risk SNPs	*APOE* Carrier status for recessive Mendelian disorders	Huntington Prion diseases ALS (SOD1)	
	Estimated number of genes/loci:	10s	10s (eventually 100s – 1000s)	1000s	10s	~20,000

Berg, Khoury, Evans, Genet Med, 2011

8

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Slide 5

DHHS3 *added bullet #3
*minor wording edits on other bullets so each bullet starts with a verb for consistency and so more active
DHHS, 12/12/2012

How do we define Actionability?

In the context of NHANES

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Evidentiary and Ethical Issues around Return of Results in WGS Analysis ACMG Recommendations

April, 2013

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]

[1]Division of Genetics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA; [2]Partners Healthcare Center for Personalized Genetic Medicine, Boston, Massachusetts, USA; [3]Department of Genetics, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, USA; [4]Division of Medical Genetics, Department of Human Genetics, UCLA School of Medicine, Los Angeles, California, USA; [5]Division of Molecular Pathology, Department of Pathology & Laboratory Medicine, UCLA School of Medicine, Los Angeles, California, USA; [6]Division of Pediatric Genetics, Department of Pediatrics, UCLA School of Medicine, Los Angeles, California, USA; [7]Department of Genetics, University of Alabama, Birmingham, Alabama, USA; [8]Department of Human Genetics, Emory University School of Medicine, Atlanta, Georgia, USA; [9]Center for Medical Ethics and Health

Evidentiary and Ethical Issues around Return of Results in WGS Analysis 56 Genes

Phenotype	MIM - Disorder	PMID - GeneReviews Entry	Age of Onset	Gene	MIM - Gene	Inheritance*
Hereditary Breast and Ovarian Cancer	604370, 612555	20301425	Adult	*BRCA1*	113705	AD
				BRCA2	600185	
Li-Fraumeni Syndrome	151623	20301488	Child/adult	*TP53*	191170	AD
Peutz-Jeghers Syndrome	175200	20301443	Child/adult	*STK11*	602216	AD
Lynch Syndrome	120435	20301390	Adult	*MLH1*	120436	AD
				MSH2	609309	
				MSH6	600678	
				PMS2	600259	
Familial adenomatous polyposis	175100	20301519	Child	*APC*	611731	AD

Evidentiary and Ethical Issues around Return of Results in WGS Analysis: EGAPP Approach

ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

April, 2013

Description and pilot results from a novel method for evaluating return of incidental findings from next-generation sequencing technologies

Katrina A.B. Goddard, PhD[1], Evelyn P. Whitlock, MD, MPH[1], Jonathan S. Berg, MD, PhD[2], Marc S. Williams, MD[3], Elizabeth M. Webber, MS[1], Jennifer A. Webster, MS[1], Jennifer S. Lin, MD, MCR[1], Kasmintan A. Schrader, MBBS[4], Doug Campos-Outcalt, MD, MPA[5], Kenneth Offit, MD, MPH[4], Heather Spencer Feigelson, PhD[6] and Celine Hollombe, MPH[1]

Purpose: The aim of this study was to develop, operationalize, and pilot test a transparent, reproducible, and evidence-informed method to determine when to report incidental findings from next-generation sequencing technologies.

Methods: Using evidence-based principles, we proposed a three-stage process. Stage I "rules out" incidental findings below a minimal threshold of evidence and is evaluated using inter-rater agreement and comparison with an expert-based approach. Stage II documents criteria for clinical actionability using a standardized approach to allow experts to consistently consider and recommend whether results should be routinely reported (stage III). We used expert opinion to determine the face validity of stages II and III using three case studies. We evaluated the time and effort for stages I and II.

Results: For stage I, we assessed 99 conditions and found high inter-rater agreement (89%), and strong agreement with a separate expert-based method. Case studies for familial adenomatous polyposis, hereditary hemochromatosis, and α1-antitrypsin deficiency were all recommended for routine reporting as incidental findings. The method requires <3 days per topic.

Conclusion: We establish an operational definition of clinically actionable incidental findings and provide documentation and pilot testing of a feasible method that is scalable to the whole genome.

Genet Med advance online publication 4 April 2013

Key Words: clinical actionability; population screening; secondary findings; whole-exome sequencing; whole-genome sequencing

Adult Incidental Findings

ACTIONABILITY

1. Is there a practice guideline or systematic review for the genetic condition?

2. Does the practice guideline or systematic review indicate that the result is actionable in *one or more* of the following ways?
- Patient Management
- Surveillance or Screening
- Family Management
- Circumstances to Avoid

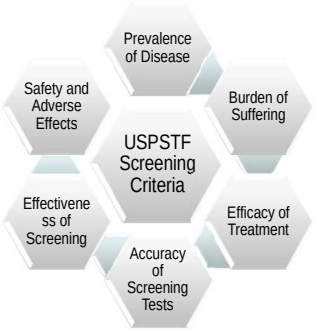
3. Is the result actionable in an undiagnosed adult with the genetic condition?

NOT ACTIONABILITY

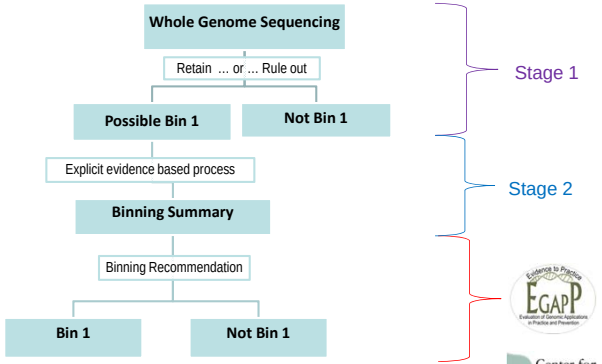
Topic	Rational for exclusion
End of diagnostic odyssey	IFs are not related to the indication for testing
Reproductive decision making	Not relevant for all patients in our clinical scenario
Personal utility: value of knowing the information	Not actionable in a clinical context

Population Screening Framework

- Wilson & Jungner, WHO Criteria, 1968
- Screening in newborns & children
  - Calonge et al., Genet Med 2010
  - Watson et al., Ment Retard Dev Disabil Res Rev 2006
- UK National Screening Committee Criteria, 2012
- Population screening programs in genomic medicine
  - Khoury et al., N Engl J Med, 2003
  - Burke et al., Epidemiol Rev, 2011
- Harris et al., Evaluating proposed screening programs, USPSTF, Epidemiol Rev, 2011



Process Overview



Stage 1: Early Rule-Out Criteria

ACTIONABILITY

1. Is there a practice guideline or systematic review for the genetic condition?

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3. Is the result actionable in an undiagnosed adult with the genetic condition?

PENETRANCE

4. Is there at least one known pathogenic variant with at least moderate penetrance (>40%) or moderate relative risk (>2.0) in any population?

SIGNIFICANCE

5. Is this condition an important health problem?

Stage 2: Criteria

Stage 1	Stage 2
Actionability	How effective are interventions for preventing the harm?
Penetrance	What is the chance that this threat will materialize?
Significance	What is the nature of the threat to health for an individual carrying a deleterious allele?
	How acceptable are the interventions in terms of the burdens or risks placed on the individual?
	Would the underlying risk or condition escape detection prior to harm in the setting of recommended care?

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Tiers of Evidence

Step 3: Determine Tier of Evidence for each Source.

First tier
- Evidence from a systematic review, or a meta-analysis, or a clinical practice guideline clearly based on a systematic review[1]

Second tier
- Evidence from clinical practice guidelines or broad-based expert consensus with some level of evidence review, but using unclear methods or using sources that were not systematically identified[1]

Third tier
- Evidence from another source with non-systematic review of evidence (e.g., GeneTest Reviews, OrphaNet, and Clinical Utility Gene Cards, opinion of a single or few (<5) experts) with additional primary literature cited

Fourth tier
- Evidence from another source with non-systematic review of evidence (e.g., GeneTest Reviews, OrphaNet, and Clinical Utility Gene Cards, opinion of a single or few (<5) experts) with no citations to primary data sources

[1]systematic review of evidence means that traditional systematic review methods are followed including: a) a clearly stated set of objectives, b) an explicit, reproducible methodology, c) systematic search that attempts to identify all studies that would meet the eligibility criteria, d) inclusion and exclusion criteria for studies are pre-defined, and e) an assessment of the validity of findings in the included studies, and f) a systematic presentation and synthesis of the characteristics and findings of the included studies. (http://www.cochrane-handbook.org/)

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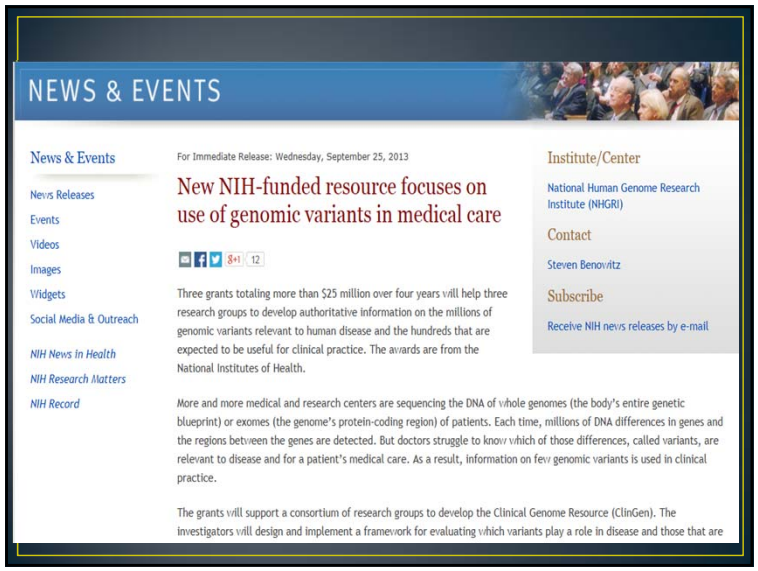

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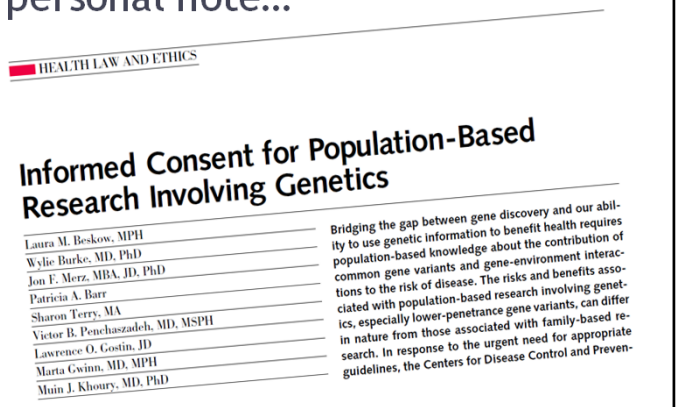
- **Issue of "opportunistic" screening**

Research Participants' Attitudes and Preferences

Laura M. Beskow, MPH, PhD
Duke University
February 10, 2014

A personal note…



HEALTH LAW AND ETHICS

Informed Consent for Population-Based Research Involving Genetics

Laura M. Beskow, MPH
Wylie Burke, MD, PhD
Jon F. Merz, MBA, JD, PhD
Patricia A. Barr
Sharon Terry, MA
Victor B. Penchaszadeh, MD, MSPH
Lawrence O. Gostin, JD
Marta Gwinn, MD, MPH
Muin J. Khoury, MD, PhD

Bridging the gap between gene discovery and our ability to use genetic information to benefit health requires population-based knowledge about the contribution of common gene variants and gene-environment interactions to the risk of disease. The risks and benefits associated with population-based research involving genetics, especially lower-penetrance gene variants, can differ in nature from those associated with family-based research. In response to the urgent need for appropriate guidelines, the Centers for Disease Control and Preven-

JAMA 2001: 286(18): 2315-21

Public support for biobanking

- Data suggest that people are supportive of population-based biobanking research
  - NHANES experience: Consent rates for future genetic research
    - 1999-2000: 85%
    - 2001-2002: 90%
    - 2007-2008: 86%

McQuillan et al 2003; 2006; 2011

Today: Participant views on return of individual genetic research results

- What do people say when asked "do you want individual results?"
- What explains their answers?
  - Reasons people give
  - Research design challenges
- Discussion: Role of participant preferences in setting policy

Literature on Participant Preferences

(references on final slide)

In general, people say 'yes' when asked if they want individual research results

- For example: Online survey of US adults (n=4659) about a proposed genetic cohort study
  - "Nine in ten agreed that they would want to know all of their individual research results"

Kaufman et al 2008

Many say 'yes' even when not actionable

- For example:
  - Online survey about proposed genetic cohort study
    - 91% wanted "individual research results about health risks, even if there was nothing I could do about them"
  - Telephone survey of older US adults (n=504) about research on stored biospecimens
    - 89% wanted to be informed if "the researcher learned something about you but wasn't sure if it might affect your health"

Kaufman et al 2008; Wendler & Emanuel 2002

What reasons do people give?

- Information is valuable
- Treatment, preventio
- Benefit family
- Reciprocity

"More than anything just to

"[To learn] if there's a way I should

"You have an obligation to tell these people. They expect something back from you. I'm

Particularly in studies that maintain ongoing contact (e.g., to obtain updated health info):

"Because if they're calling you up and wanting to find out how your health is, it seems to me like they could mention something."

Murphy et al ... *013*

What reasons do people give?

- Future treatment
- Research
- Life planning
- Right to informati

"You might as well know because

"If somebody has an interest in working on a research project with

"Yeah, because that's their blood. They have a right to know what's going on. If I sat down and … willingly gave somebody some of my blood for a test, I think I should get it back. I should know the grade of my test since I took it."

Murphy et al

What reasons do people give for not wanting results?

- Undue worry, distress
- Misunderstanding
- Nature of the resea

"I wouldn't want to be told … because

"The average person is not gonna be

"If they're giving you some type of drug or a placebo, then … they'd be obligated to tell you. But if all they're doing is taking your blood and your general information, and then watching you from a distance, they're under no obligation to come back to you."

Research Design Challenges

The effect of asking

- "Involuntary curiosity": Curiosity arises spontaneously when individual alerted to information gap
  - Posing a question that confronts individual directly with missing information
  - Possession of information by someone else

Loewenstein 1994

The effect of asking

Example: Survey of research participants (n=561)

- "Suppose you could order a free home test kit that would allow you to easily and painlessly test your saliva to determine your chances of devel… would you be to orde…
  - **39%** said 'very like…
- "Suppose as part of a… test on your blood, ar… Alzheimer's. How lik… the results?"
  - **70%** said 'very likely'

- "I wouldn't seek out such information, but if it's available, I would want to know it."
- "Because if I knew for a fact that someone knew, then I would want to know."

Wendler & Pentz 2007

What we ask (and don't ask)

- Preferences versus acceptability
- Example: Cognitive interviews (n=40) about biobank consent form
  - Asked: "What do you think about the statement, 'You should not expect to get individual results from research done with your blood'?"

Beskow et al 2008; 2009

What we a…

- ~2/3 said th…
  - Limited…
  - Differe…
  - Lack of prior expectations

"It just takes too much time trying to b… that… stu… awa…

"[It's] supposed to be a research thing. It's not like a medical treatment that they have to tell you there's something in there. It's a random blood test -- not diagnosis or …

"This is a collective thing, you know. I really understood that from the very beginning."

"If there is an option for me to get results, I'm going to say yes. But if you tell me I'm not going to get them, I'm not really going to care." *(Bollinger et al 2012)*

How we ask, Part 1: Wording

- Example:

  "Assume a genetic test was performed in the future using your stored tissue samples that were taken now to determine your chances of getting a particular illness (*e.g.*, cancer, diabetes, depression). How much would you want to be given the results of the test at time the future test is done?"

  - 71% answered at 'very interested' end of 11-pt scale

Hoop et al 2009

How we ask, Part 2: Hypotheticals

- Used to anticipate public interest, understand factors that influence reactions, prepare for emerging technologies
- Responses to hypotheticals may not accurately reflect actual behavior (*e.g.*, sizeable gap between estimated and actual uptake of genetic susceptibility testing)

Persky et al 2007

How we ask, Part 3: Context

- Contextual circumstances influence the way participants perceive, position themselves towards biobank research
- Participants acquire different expectations depending on the type of biobank, type of relationship

Hoeyer 2010

The context of Kaufman et al.

- Cohort study investigating genes, environment, lifestyle:
  - 10 or more years duration
  - First study visit at local medical facility (community clinic, hospital)
  - Give detailed medical history, including diet and lifestyle
  - Asked about home, workplace environmental exposures
  - Complete physical appropriate for age, give blood sample
  - Perhaps asked to keep food, exercise diary; use device to measure environmental pollution
  - Contacted for updated info every 6-12 months: General health; new illnesses; lifestyle, diet changes; environmental exposures
  - Second physical exam at end of study
  - Researchers apply to study coded samples, genetic information, and other medical data stored at NIH

Kaufman et al 2008

The context of Kaufman et al.

- Further context – definition of "individual research result":

> An individual participant's research result would be the information about whether that person had a specific genetic, environmental, or lifestyle risk factor

  - 91% agreed "I would want to know all of my individual research results about health risks, even if there was nothing I could do about them"

Kaufman et al 2008

The Role of Participant Preferences

Summary

- Literature on participant preferences
  - Provides important, interesting insights
  - Limitations of empirical research
    - Importance of making survey/interview instruments routinely available with publication
- Key question: What is the role of participant preferences in setting policy specifically in the NHANES context?

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