National Health and Nutrition Examination Survey

Logistics of Returning Genomic Results

Kathryn S. Porter, M.D., M.S.
Director
Division of Health and Nutrition Examination Surveys

National Center for Health Statistics
Division of Health and Nutrition Examination Surveys

Returning results

Navigate the ethical and logistical issues of reporting a "clinically actionable" result **years** after blood was collected

Are results valid?

Returning results

Need two plans:

- Retrospective

  Previously consented: develop procedures for returning results given the consent stated no results reported

- Prospective

  New consent language

Previously consented

- Documented consent obtained between 2 and 23 years ago; n=26,000
- What participants agreed to:

  20-23 years ago:

  Store blood for future testing (*no mention of genetic studies or return of results on consent)*

  2-14 years ago:

  Store DNA for future studies and no return of results

Previously consented

- No active tracking of participants
- Special Projects Branch (SPB), Office of Analysis and Epidemiology (OAE), NCHS:
  - Passive tracking of NHANES participants by change-of-address postal checks
  - Linkage to mortality files (vital status)
- No ongoing assessment of the validity of addresses for NHANES participants

Option: re-contact by mail

What would the letter say?

You were a participant in NHANES

A sample of your blood was banked for genetic studies

We have changed our policy governing the use of NHANES DNA specimens…..From now on, the NHANES program will contact you when your results from genetic studies may be important for you know. You will be sent a letter describing the study and a toll free number to call if you want your individual genetic results.

~Phone number for questions or opting out~

Process

- Determine the clinically actionable variants and reassess annually
  - Recruit and convene a Medical Advisory Panel: clinicians, research scientists, bioethicists, and genetic epidemiologists
- Reopen DNA bank to new research proposals, update the Federal Register notice

Process

- Work with researchers to produce plain English (Spanish) reporting letters
- Design procedures for participants who don't speak English or Spanish
- Hire a genetic counselor to support operations (? - $)
- Enhance computing infrastructure to handle genomic data (? -$)

The road ahead

Prospective

Two plans:

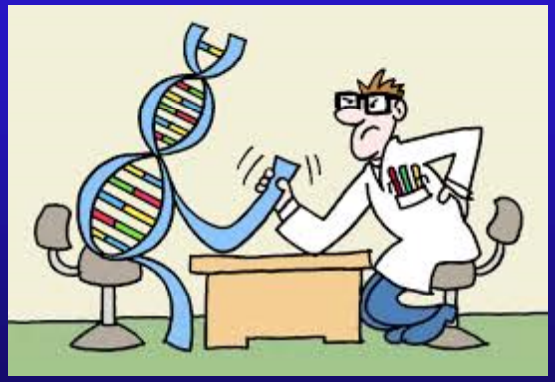
- Restart collecting and storing DNA specimens ($)
  - New consent going forward with statement about return of results
  - Previously mentioned survey support operations apply

Prospective

- Whole genome sequencing as part of the NHANES data collection (? - $)
  - Funding partners needed
  - Must meet all criteria for approving new content in NHANES
  - Must be able to assure confidentiality
  - Must have an advanced computing infrastructure to handle genomic data (? -$)
  - Must have skilled staff

Final note

- All changes to the NHANES Protocol and the plan to make DNA available to researchers must be reviewed and approved by:
  - NCHS Human Subjects Contact
  - NCHS Confidentiality Officer
  - NCHS Research Ethics Review Board



Thank you

nhanes

Returning Incidental Findings: Retrospective vs. Prospective Collections

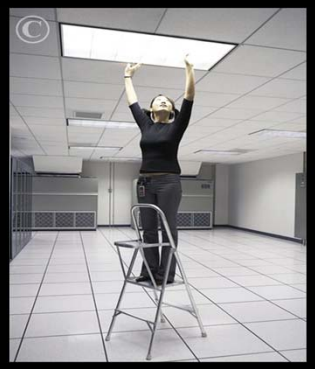
Kelly Edwards, PhD Bioethics
University of Washington
Schools of Medicine and Public Health

Key Concepts to Consider

- Expectations
- Respect
- Reciprocity
- Transparency

We are governed by laws, technologies, markets, and norms. - Larry Lessig

Up to us to set standards of excellence



Regulations set the floor for behavior

Where do expectations come from?

We think:

- Consent form

In practice:

- Experience
- Assumptions
- Hopes
- Misunderstandings
- Miscommunications

Key differences between retrospective and prospective collections

Previously collected:

- We didn't communicate about returning results (or said we would NOT)
- The person may or may not know they are in a database
- It may be impracticable to find people

Going forward:

- We could communicate more clearly and leave options open
- We could make explicit the purpose of collection
- We could set up a tracking and communication system

Are these moral differences? Do we have obligations either way?

National Research Council 2012

Committee on the Review of the Appropriate Use of AFIP's Tissue Repository following Its transfer to the Joint Pathology Center 2011-2012

James F. Childress, PhD *Chair*
University of Virginia

Alexander M. Capron, LLB
University of Southern California

Carolyn C. Compton, MD, PhD
Critical Path Institute

Kelly Edwards, PhD
University of Washington

Bradley A. Malin, PhD
Vanderbilt University

Guido Marcucci, MD
Ohio State University

Robert L. Reddick, MD
University of Texas Health Science Center

Frederick J. Schoen, MD, PhD
Harvard Medical School

Michael L. Shelanski, MD, PhD
Columbia University

Robert West, MD, PhD
Stanford University Medical Center

Ignacio I. Wistuba, MD
University of Texas M.D. Anderson Cancer Center

Susan M. Wolf, JD
University of Minnesota

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Advising the nation / Improving health

Retrospective Use of an Existing Collection

- Re-consent is impracticable
- Research should use de-identified data/specimens primarily
- A third party should review all access requests (and returning results case-by-case considerations)
- General findings and aggregate results should be posted publicly and accessibly
- Opting out of future research should be straight-forward

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Advising the nation / Improving health

Need for responsive governance and policies

The status quo to research on stored specimens and data is being reconsidered by policymakers due to:

- increasing capabilities for reidentification of genetic material raise concerns about the adequacy of deidentification measures.
- emerging public opinion suggests that research to which a source did not consent can be concerning even when material is deidentified.
- legal challenges to research use of clinically derived material indicate growing concern over research use without consent.

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Advising the nation / Improving health

Do Researchers Have an Obligation to Give Anything Back to "Participants"

Clinical Translational Science Awards
Ethics and Regulatory Committee
Biobank Working Group 2012

Arguments Against Obligation

Intrinsic:

- People are altruistic
- People have an obligation to participate (have already received benefits from past research)
- Need clear lines between clinical and research

Instrumental:

- Costs to other duties like doing good science
- Bank is so far removed from donors
- Not skilled or resourced to meet this duty

Arguments for Obligation

Intrinsic:

- Demonstrates respect
- Provides benefit (when other payoffs are far away)
  - Particularly as we are asking you to incur risks
- Is more equitable (we benefit, you benefit)
- Enacts reciprocity

Instrumental:

- Can encourage participation and support
- Builds or sustains trust
- It might save your collection
- We should because we can

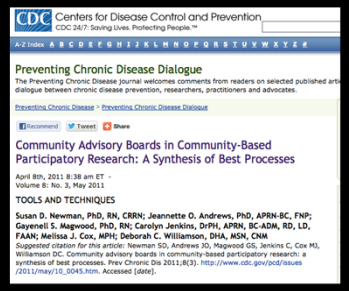
What can collections give back?

What will discharge the duty to give back? How and when this should be discharged? To whom? Who decides? What could collections give back?

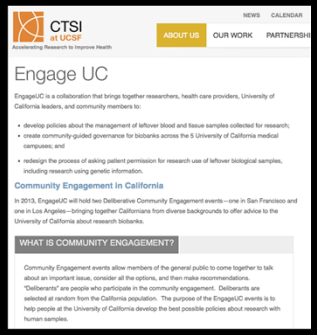
- Gratitude - thanks
- Money at recruitment
- Basic health information at recruitment
- Information about where samples and data go
- Information about how samples/data are handled
- Opportunities to learn (enhanced science literacy)
- Aggregate results from research uses (health literacy)
- Benefit sharing – feeding resources back into patient care or community

Community Input

Community Advisory Boards

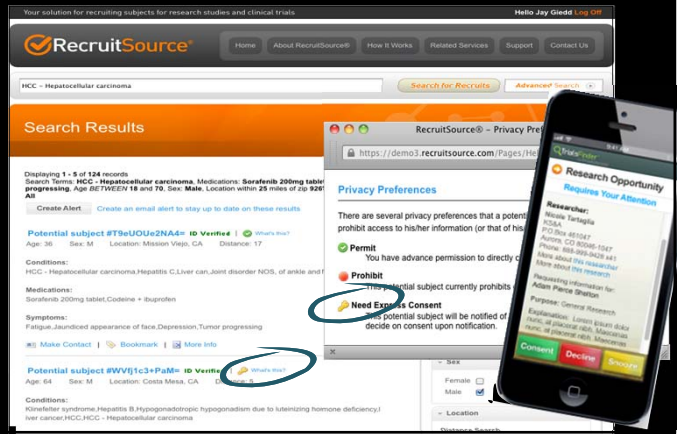


Community Deliberation



PEER: Platform for Engaging Everyone Responsibly

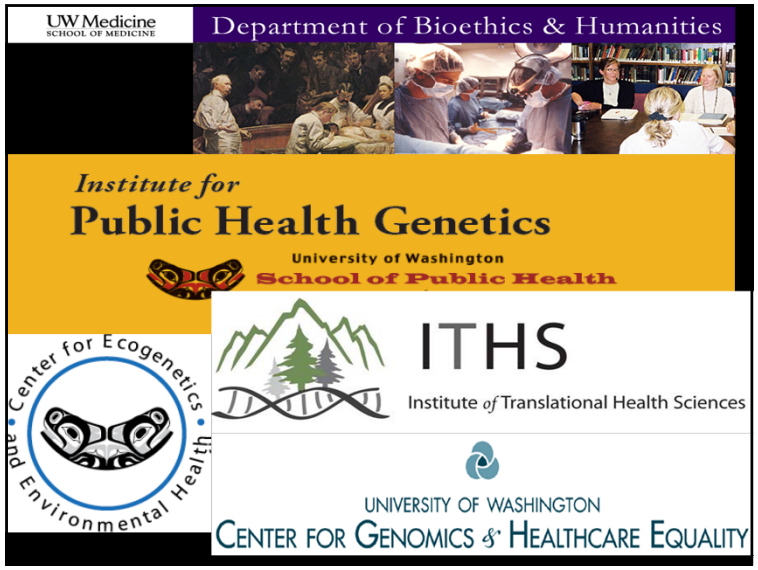
A Genetic Alliance Initiative, powered by Private Access technology.



Privacy

- Privacy entails people's right to make decisions about intimate matters.
- Including who has access to their data, for what purposes.

– 1890 Warren & Brandeis


UW Medicine
SCHOOL OF MEDICINE
Department of Bioethics & Humanities
Institute for
Public Health Genetics
University of Washington
School of Public Health
Center for Ecogenetics and Environmental Health
ITHS
Institute of Translational Health Sciences
UNIVERSITY OF WASHINGTON
CENTER FOR GENOMICS & HEALTHCARE EQUALITY

NATIONAL HUMAN GENOME RESEARCH INSTITUTE Division of Intramural Research

Practical Aspects of Returning Genome Results

Barbara Bowles Biesecker, PhD, MS

Practical Aspects to Consider

- What would be entailed to consent NHANES participants?
- How would participants be helped to decide if they wanted to learn results?
- How would they be returned?
- How will participants be helped to act on the results?

Did NHANES participants consent to receive genomic information?

- No
- They can be retroactively consented
- Provides an opportunity to help set expectations and mitigate unrealistic ones
- People can appreciate the uncertainties and tentative nature of some of the information; and they can appreciate the duality of genetics and behavior in determining causal beliefs

What have we learned about consent to receive genomic information?

- ClinSeq consent, participants learned key information about sequence information and its implications (Kaphingst et al, *Clin Genet*)
- Trust is high in the researchers to keep their information private (Jamal et al, *EJHG*)
- Parents of affected children readily engaged in conversations about secondary variants (Sapp et al, *Clin Genet*)
- ClinSeq Interview Study (analyzing data now)
- RCT of two models of consent to sequencing (ongoing)

Do NHANES participants want genome Information?

- Maybe?
- Research suggests more likely yes than no
- It will depend on their expectations and prior experiences with genetic testing (if any)
- They can be helped to understand it as a source of health related information with implications for themselves and close relatives

What do early studies suggest?

Studies of NIH research participants indicate that they want the information

- ClinSeq participants interested in learning results of all types, with greater interest in actionable variants and carrier results (N=322)
- Parents of children enrolled in NIH studies eager to learn secondary variants (N=25)
- Studies of NIH Multiplex Initiative participants demonstrated interest in health risk information

Facio et al, *EJHG,* Wright et al, *GIM,* Sapp et al, *Clin Genet*

Era patient/citizen advocacy/rights

- Era of partnerships and transparency in health care delivery—access to one's medical record
- Staying healthy and taking personal responsibility (at least among the educated and well off)
- Data suggest that if information about one's health becomes knowable, people want to know it—at least they want the choice presented
- Value found in knowing what we can about ourselves

Will NHANES participants learn the information?

- Maybe?
- Research suggests more likely yes than no
- Personalized nature of the results make them notable –depends on what is entailed
- Way they are returned suggests they are distinct from other medical tests
- What are the priorities of what they need to learn? Estimated risks, prevention or early treatment options, referrals to specialists

What does early research suggest?

- Recall of receipt of results high (ClinSeq)
- Among parents of affected children also
- Seem to have little anxiety or concern about having learned results—most grateful
- They have communicated findings to relatives at risk
- Participants may learn certain findings as effectively from a web-based or internet platform (studies underway)

Will NHANES participants use the information?

- Maybe?
- Research suggests more likely no than yes
- Likely to tell their providers who can help insure that they follow up on recommendations
- Even with evidence-based interventions it's hard to get people to change their health-related behavior
- Participants may still value the information—personal utility

What does research suggest?

- ClinSeq participants who received results told their partners, siblings and providers their results
- None had changed their health care or lifestyle as result
- Pleased to have the information—see its potential
- Similarly parents so far (ongoing) interested to learn carrier results on affected children

Role of Genetic Counselors

- Consenting participants in most sequencing studies and clinically
- Facilitating decisions whether to learn results
- Currently involved in return of results—most often done in person
- Involved in follow up—implementation of medical recommendations, communication with relatives, communication with provider(s)

Evidence for the need for genetic counselors?

- Limited
- History of translating early use of genetic technologies
- RCT of alternative models for returning results and mastering their implications
- Need to be innovative about ways to enlist a broader range of health care providers in return and follow up to results.

Risks of genome information?

- Misunderstanding of the information and its implications
- Ignore something that can be prevented/treated
- Fail to transmit information to at risk relatives
- Interpret a lack of information as a healthy report—false reassurance

Benefits of genome information?

- Mitigate genetic risk for disease
- Mitigate similar risks to relatives
- Identify cause of current symptoms/phenotype
- Avoid adverse drug response
- Share carrier results for additional family testing and in a subset, reproductive planning
- Learning a genetic risk in the absence of a family history

Professional/Personal Bias

- People can make informed decisions to receive results
- Are largely capable of assessing its value
- Are not likely to be unduly traumatized by information
- Participants should have choices
- It seems to be the “right thing to do” for a subset of results
- Consider NHANES participants their partners