

National Health and Nutrition Examination Survey

Logistics of Returning Genomic Results

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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:

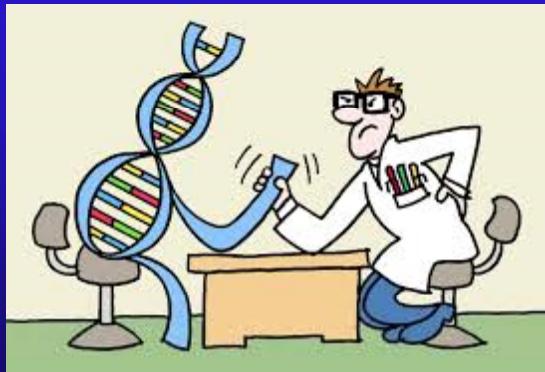
- Restart collecting and storing DNA specimens (\$)
 - New consent going forward with statement about return of results
 - Previously mentioned survey support operations apply

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





Returning Incidental Findings: Retrospective vs. Prospective Collections

Kelly Edwards, PhD Bioethics
University of Washington
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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

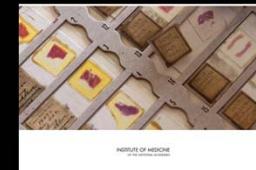
Going forward:

- 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?



Future Uses of the Department of Defense Joint Pathology Center Biorepository



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

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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 straightforward

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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.

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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

CDC Centers for Disease Control and Prevention
CDC 24/7 Saving Lives. Protecting People.™

A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Preventing Chronic Disease Dialogue
The Preventing Chronic Disease journal welcomes comments from readers on selected published articles. The dialogue between chronic disease prevention, researchers, practitioners and advocates.

[Preventing Chronic Disease](#) > [Preventing Chronic Disease Dialogue](#)

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Community Advisory Boards in Community-Based Participatory Research: A Synthesis of Best Practices

April 8th, 2011 8:38 am ET
Volume 8: No. 3, May 2011

TOOLS AND TECHNIQUES

Susan D. Newman, PhD, APRN-BC, FNP; Gaynor S. Andrews, PhD; Carolyn Jenkins, APRN, BC-ADM, RD, LD, FNP; Mary J. Cox, MPH; Deborah C. Williamson, DHA, MSN, CNM
Suggested citation for this article: Newman SD, Andrews JO, Maywood GS, Jenkins C, Cox MJ, Williamson DC. Community advisory boards in community-based participatory research: a synthesis of best practices. *Prevent Chronic Dis* 2011;8(3):1-16. http://www.cdc.gov/pcdd/Issues/2011/may/10_0045.htm. Accessed [date].

Community Deliberation

CTSI **UCSF**
Assessing Research to Improve Health

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Engage UC
EngageUC is a collaboration that brings together researchers, health care providers, University of California leaders, and community members to:

- develop policies about the management of leftover blood and tissue samples collected for research;
- create community-guided governance for biobanks across the 5 University of California medical campuses; and
- redesign the process of asking patient permission for research use of leftover biological samples, including research using genetic information.

Community Engagement in California
In 2013, EngageUC will host two Deliberative Community Engagement events—one in San Francisco and one in Los Angeles—bringing together Californians from diverse backgrounds to offer advice to the University of California about research biobanks.

WHAT IS COMMUNITY ENGAGEMENT?

Community Engagement events allow members of the general public to come together to talk about an important issue, consider all the options, and then make recommendations. "Deliberants" are people who participate in the community engagement. Deliberants are selected at random from the California population. The purpose of the EngageUC events is to help people at the University of California develop the best possible policies about research with human samples.

PEER: Platform for Engaging Everyone Responsibly

A Genetic Alliance Initiative, powered by Private Access technology.

Your solution for recruiting subjects for research studies and clinical trials

RecruitSource®

Hello Jay Giordi Log Off

HCC - Hepatocellular carcinoma

Search Results

Displaying 1 - 5 of 124 records

Search Terms: HCC - Hepatocellular carcinoma, Medications: Sorafenib 200mg tablet progressing, Age: BETWEEN 18 and 70, Sex: Male, Location within 25 miles of zip 92017

[Create Alert](#) [Create an email alert to stay up to date on these results](#)

Potential subject #T9eUOUe2NA# ID Verified | [View this?](#)

Age: 36 Sex: M Location: Mission Viejo, CA Distance: 17

Conditions: HCC - Hepatocellular carcinoma Hepatitis C,Liver can,Joint disorder NOIS, of ankle and foot

Medications: Sorafenib 200mg tablet, Codeline + Ibuprofen

Symptoms: Fatigue,Jaundiced appearance of face,Depression,Tumor progressing

[Make Contact](#) | [Bookmark](#) | [More Info](#)

Potential subject #WVj1c3+PaM# ID Verified | [View this?](#)

Age: 46 Sex: M Location: Costa Mesa, CA Distance: 17

Conditions: Hepatitis syndrome,Hepatitis B,Hypogonadotropic hypogonadism due to luteinizing hormone deficiency,Iver cancer,HCC,HCC - Hepatocellular carcinoma

Search Results

Privacy Preferences

There are several privacy preferences that a potential subject can have that prohibit access to his/her information (or that of his/her family members).

Permit
You have advance permission to directly contact me.

Prohibit
This potential subject currently prohibits me from contacting him/her.

Need Express Consent
This potential subject will be notified of my attempt to contact him/her and I will decide on consent upon notification.

[Consent](#) [Decline](#) [Logout](#)

Sex: Female Male
Location: Costa Mesa, CA

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





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Practical Aspects of Returning Genome Results

Barbara Bowles Biesecker, PhD, MS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES | NATIONAL INSTITUTES OF HEALTH | genome.gov/DIR

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?



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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



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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)



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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



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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



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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*



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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



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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)



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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



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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



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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)



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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.



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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



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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



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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



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