NHANES Genetics Program Update

September 2012

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Health Statistics

Presentation Objectives

- Recap Feb 2012 BSC input to NHANES Genetics Program

- Updates since Feb 2012
  - Consent research
  - DNA collection 2013-14
  - Affymetrix Genome–Wide Human SNP Array 6.0 chip binning results
  - Published guidance re: genetic research for biobanks and archived datasets
  - Exploring outreach meeting for broader comment on NHANES Genetics Program

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Feb 2012 BSC input to NHANES Program

- Pre-test genetics consent changes to include the option of receiving genetic results
- Report back genome binning progress
- Formulation of BSC workgroup to determine genes meeting NHANES ‘dire duty to warn’ criteria
- Outreach to other organizations for broader discussion of genetics program issues raised

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Pre-test genetics consent changes

- Staffing losses in ORM QDRL resulted in timeline shift to late summer 2012 for pilot test of genetic consent/re-contact letter changes
- This timeline would not allow changes to 2013-14 consent documents

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DNA collection 2013-14

- Funding for 2013-14 DNA collection
  - The genetic specimen processing is jointly funded by NCEH and NCHS
  - Budget considerations, combined with time delays to modify the genetic consent resulted in the joint NCHS and NCEH decision to discontinue DNA specimen collection for the 2013-14 data cycle

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Affymetrix 6.0 Chip binning

Affymetrix Genome–Wide Human SNP Array 6.0 chip binning results

- Binning analysis of SNPs on Affy 6.0 array according to Berg et al 2011 binning algorithm
- SNPs in Affy 6.0 array schema annotated with minor allele frequencies from 1000 Genomes Project
- SNPs with allele frequencies < 5.3% annotated using NCBI dbSNP

Categorizing Potential Genetic Results

Binning by Loci - Berg. *Genetics in Medicine* (2011)

Bin 3 - genes of unknown clinical implication

Bin 2 - variants within genes that are clinically valid but not directly actionable

Bin 1 - variants within genes that have direct clinical utility based on professional organization diagnosis and treatment guidelines

Only Bin 1 variants should be considered for reporting

Affymetrix 6.0 Chip binning continued

SNPs then binned based on genes annotated in, and then noted reportable if <5% allele frequency and

- Annotated in HGMD as disease mutation, or
- Truncating (nonsense, frameshift, splice site

Results

- No clearly reportable Bin 1 SNPs
- 3 possibly reportable SNPs

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Recommendations for biobanks conducting genetic research

Managing incidental findings and research results in genomic research involving biobanks and archived data sets. Wolf et al, Genetics in Medicine 2012; 14:361-384.

- 2-year NIH funded project analyzing the responsibilities involved in managing ROR in a biobank research setting
- Multidisciplinary working group (genomic research, biobank management, medicine, law, bioethics)
- 4 meetings held, including representation from NIH funded researchers, CLIA, ISBER, and a public conference presenting draft recommendations

Recommendations for biobanks conducting genetic research, cont'd

1. Biobank system should fulfill IF/IRR responsibilities
2. Develop explicit policy on IF/IRR return
3. Biobank CARR responsibilities
   - Clarify criteria for evaluating returnable findings
   - Analyze individual findings in relation to this
   - Re-identify contributor
   - Re-contact contributor to offer the finding

Recommendations for biobanks conducting genetic research, cont'd

4. Findings that are analytically valid, CLIA-certified, with substantial risk of serious health condition, and clinically actionable should generally be offered to consenting contributors
5. n/a for archived data setting
6. Maintain capacity for re-identification of contributors over an extended time period

Recommendations for biobanks conducting genetic research, cont'd

7. Anticipate how to handle recontacting contributors with IF/IRR
   - Reflect in consent
   - Capacity and expertise for recontact and communication of findings
   - Understandable to contributor, plus information on clinical referral (genetic counseling)
8. Conduct research on preferences, experiences and outcomes of participant populations with return of IF/IRRs

Recommendations for biobanks conducting genetic research, cont'd

9. Communicate aggregate results (journals and other media accessible by participants), and consider how to respond to follow-up inquiries about the importance of aggregate findings
10. Ensure biobank guidelines and budget adequately supports responsible management of IF/IRRs

May 2011 NHANES Genetics Program Workshop Highlights

- **Panel of experts**
  - intra/extra mural experts
  - geneticists/bioethicists
- **What results should be reported back – are standards or guidelines available?**
- **How to determine and operationalize criteria for clinically relevant genetic findings with a dire duty to warn threshold?**
- **Who determines ROF threshold?**
- **How/When to report back?**

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Outreach meeting for broader comment on NHANES Genetics Program

Objective

- To highlight and identify the challenges and options for returning individual results from genomic research using population-based banked specimens

Conduct under the auspices of NAS/IOM

Draft workshop proposal developed

Outreach meeting for broader comment on NHANES Genetics Program, cont'd

Participants

- Must include investigators from large studies with a population/epidemiology focus which collect specimens analyzed for genomic research
- Must include bioethicists and medical geneticists

Timeline

- Conduct workshop with publication of workshop summary by summer 2013

Outreach meeting for broader comment on NHANES Genetics Program, cont'd

Session 1 Focus - Overview

- Current practices and changing recommendations for reporting back results from genomic research in population-based research studies

Outreach meeting for broader comment on NHANES Genetics Program, cont'd

Session 2 Focus - What findings are returnable

- Acceptable criteria for determining which findings are returnable, e.g. 'binning the genome'
- Acceptable procedures for determining returnable findings for population research studies, e.g. BSC subcommittee vetting of returnable findings in NHANES context
- Should non clinically-actionable conditions with reproductive implications be considered for return to participants of population research studies?
- Should consideration be given for a 'statute of limitations' for return of genomic research findings on archived specimens?

Outreach meeting for broader comment on NHANES Genetics Program, cont'd

Session 3 Focus - How to implement the return of findings to participants

- What is acceptable consent language for participants being enrolled prospectively regarding IRR?
- Does this change for participants with banked specimens who were consented under a non-return policy?
- What are acceptable procedures for reporting results to participants (e.g. in writing, by phone, expertise, etc)?
- What are acceptable modes of communicating aggregate results of genetic findings (e.g. newsletters, website, etc)?
- What is an acceptable level of response to participant requests for genetic findings with no known health or reproductive importance?

Thank You

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