Motivators for Participation in a Whole Genome Sequencing Study: The ClinSeq Experience

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“... complex, groundbreaking, and multidisciplinary research is still needed before personal genomics reaches the mainstream of medicine.”
Opportunity at the NIH

- NHGRI has a long-term goal of developing the technology and infrastructure for LSMS for health research

- Pilot studies are needed to develop and implement LSMS in a research setting

- Only direct sequencing can assess the relative contribution of rare vs. common variants to the architecture of common disease
What is the ClinSeq project?

- Pilot whole genome sequencing to assess the feasibility of using the technology, interpreting large amounts of data & returning results
- Functional regions of 400 candidate genes for coronary heart disease
- Aims:
  - Develop infrastructure for generating, interpreting, and returning medical sequencing data
  - Investigate technical, medical, and genetic counseling issues of implementing such technology
Study Cohort

- Target: 1,000 participants
- Non-smokers 45 to 65 years of age
- Phenotyped for Coronary artery disease
What is unique about ClinSeq?

- Research participants provide informed consent for whole genome sequencing
- Research participants can choose to receive individual genotype results that are determined to be clinically significant
Aims of Motivation Study

- To explore participants’ expectations of what could be learned from testing many genes
- To explore the reasons individuals participate in a whole genome sequencing study, such as ClinSeq
Methods

Initial Visit:

Survey completed by participant re: Expectations of WGS
Reasons for participating in ClinSeq
Demographic (eg: gender, race, ethnicity)

Blood draw for clinical tests (eg: lipid profile)
and for genomic analysis

EKG
Vital Signs

Genetic Counseling and Informed Consent
(including review of family history)

Medical History

Echocardiogram

MDCT
(Calcium Score)
Pre-consent survey

Testing for many genes can… (Check all that apply)

☑ Find a genetic risk for a disease that you do not have, but could develop in the future
☑ Find a genetic cause or contribution for a disease that you have
☑ Give you a “clean bill of health”
☑ Give you information about not only you, but also your relatives
☑ None of the above
☑ Don’t know

1. What else, if anything, could be learned from testing many genes?

2. What are your reasons for wanting to participate in this study?
Analysis

- Responses to the closed-ended question were summed.

- Responses to the open-ended questions were coded in NVIVO 7 using two different conceptual codebooks.

- Codebooks were revised through an iterative process until the most concise codes were achieved.

- A primary coder coded all of the responses and a secondary coder coded 25-33% of the responses.

- Inter-coder reliability was high (~ 95%).

- Major themes were identified and are illustrated with quotes from the participants.
Results

Participants enrolled between January 2007 and May 2008
n=337

96% (322) completed survey
Age
n=322

Mean age = 57
Gender
n=322

Female 55%

Male 45%
Race
n=322
Education
n=322

- College Graduate: 32%
- Post Graduate: 52%
- < College: 15%
- No response: 1%
Household Income
n=322

- < 100,000: 29%
- > 100,000: 67%
- No response: 4%
Pre-consent expectations: Multiple-choice question

<table>
<thead>
<tr>
<th>Testing many genes can... (Check all that apply)</th>
<th>No.</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>1. Find a genetic risk for a disease that you do not have, but could develop in the future</td>
<td>305</td>
<td>95</td>
</tr>
<tr>
<td>2. Find a genetic cause or contribution for a disease that you have</td>
<td>284</td>
<td>88</td>
</tr>
<tr>
<td>3. Give you a “clean bill of health”</td>
<td>26</td>
<td>8</td>
</tr>
<tr>
<td>4. Give you information about not only you, but also your relatives</td>
<td>250</td>
<td>78</td>
</tr>
<tr>
<td>5. None of the above</td>
<td>1</td>
<td>0.31</td>
</tr>
<tr>
<td>6. Don’t know</td>
<td>4</td>
<td>1.2</td>
</tr>
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- 218/322 (68%) chose options 1, 2, and 4 simultaneously
Pre-consent expectations:
What else, if anything, can be learned from testing many genes?

- 191/322 (59%) responses

- Major theme (74%): improve our understanding of genetics in the context of health

  “Predisposition to disease and other factors affecting health and quality of life.”

  “Gain more knowledge and research regarding disease entities and ways to prevent illnesses.”
Theme: Genetics & Health

- Disease cause and development
  - relationship between genes and disease
  
  “Which genes, or combinations of genes predispose individuals to certain illnesses.”

- Advancement of treatment, diagnoses, or cures
  - advancement of tailored medicine or pharmacogenomics

  “Could lead to methods for tweaking treatments and anticipating onset of disease.”
Pre-consent reasons for participation:
What are your reasons for wanting to participate in the study?

- 313/322 (97%) responses

- Two major themes:
  - altruism (45%)
  - seeking health information for self (55%)

- Minimal overlap observed between these two themes
Theme: Altruism

- General:
  "I’ve always been interested in participating in a study to help others. I enjoy reading about research and why things happen."

- Contribute to research about genetics:
  "To provide scientists/clinicians an opportunity to study my genes to help in getting answers for others."
Theme: Seeking health information for self

- Information about a **specific health condition**:
  
  “To learn about my health and risk of heart disease.”
  “To find a genetic cause for the disease that I have.”

- Information about **genetic risk**:
  
  “Concern regarding genetic risk for heart disease.”

- **Family history of disease**:
  
  “Heart disease runs in family. Curious about own genes…”
  “I am adopted and have no family history so I think I could learn things.”
Discussion

- Reasonable understanding of what could be learned from whole genome sequencing
- Sophisticated understanding of how whole genome sequencing could improve knowledge of disease cause and treatment
- ClinSeq participants share motivations with both individuals who participate in research in general, as well as with those who come forth for genetic studies

"personal health benefits" is a common motivation for participation in genetic testing studies among disease cohorts
Limitations

- Study cohort:
  - High socio-economic status
  - Consistent with literature on early adopters of new technology
  - Future studies to examine other cohorts

- Descriptive exploratory study
Implications and Future Directions

- First large cohort to consent to whole genome sequencing with the option of receiving individual genotype results
- Unique opportunity to explore emerging themes in the context of personalized genomics research
- Future studies to:
  - Measure conceptual understanding of whole genome sequencing
  - Assess attitudes/intentions towards receiving genotype results
  - Determine predictors of decisions to receive genotype results
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