Implementing Informed Consent for Genomic Research in a Large Healthcare System

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New Era of Precision Medicine

• Opportunity to fuel major advances in care of our patients and research by investigator community

• Partners HealthCare decides to invest in and launch institutional biobank of biospecimens linked to EHR

• Goal: recruit and enroll broad spectrum of patients throughout the system (Initial target: 75,000)

• How to optimize the operational issues and consent process?
Investigator Perspective

• Consent Process
  • Opt-out method, OR
  • Broad written consent process?

• Recruitment
  • Can we approach patients without going through clinicians?

• Past Experience
  • What are other internal and external biobanks doing?
  • What has been successful?

• Operational Issues
  • Do we have adequate support?
  • What resources will require IRB approval?

• Consent for re-contact
  • Integral to mission of the biobank
IRB Perspective

- **Consent**
  - Fully consented specimens to allow optimized broad use
  - Broad use of specimens (Health/Biomedical research)
  - Use of identifiable health information
  - Recontact for future studies

- **Recruitment**
  - Non-targeted approach
  - Children excluded except through collaborative studies

- **Operational Issues**
  - Recruitment materials, outreach, data/specimen management, tracking, consent process
Solution

- Collaborative development
  - Monthly meetings with IRB leadership
  - Engage Office of General Counsel
  - Created IC Task Force—reviewed 15 institutions’ approach
  - Created tissue repository language and other framework that could be used across institution, best practices.

- Direct approach approved (no targeting by patient characteristics)

- Broad consent approved

- Investigators may query and access de-identified phenotypic data, samples, genomic data without IRB review (MTAs, DUAs)
Electronic Informed Consent (eIC): Investigator Perspective

• A unique opportunity to efficiently scale enrollment without increasing costs, staffing, recruitment space
• May provide more time for decision-making about consent
• Other systems had used “opt-out” approach but we were committed to full informed consent process
• What elements and IT systems are needed? How do we ensure adequate informed consent?
• How often can we contact patients to invite participation?
Electronic Informed Consent (eIC): IRB Perspective

• Investigate regulatory and legal issues involved in eIC, including patient authentication, electronic signature validation.

• Need to develop videos and web-based materials to educate and achieve informed consent

• Consider patient burden in context of email invitations

• Don’t over-promise in electronic materials because there is no direct benefit to participants.
Solution

• Comprehensive website with written and video descriptions of study, privacy protections and informed consent

Article

Implementation of Electronic Consent at a Biobank: An Opportunity for Precision Medicine Research

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Solution

Figure 2. Overview of workflow for eIC at the Partners Biobank.
Response rates

Table 1. Results of the email campaign (June 2014–January 2016).

<table>
<thead>
<tr>
<th>Rate of Consent by Emailed Patient</th>
<th>Patients</th>
<th>Consent Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>First email</td>
<td>184,387</td>
<td>1.5%</td>
</tr>
<tr>
<td>Second email</td>
<td>163,238</td>
<td>1.4%</td>
</tr>
<tr>
<td>Third email</td>
<td>114,327</td>
<td>1.1%</td>
</tr>
<tr>
<td>Fourth email</td>
<td>12,881</td>
<td>1.0%</td>
</tr>
<tr>
<td>Any email</td>
<td>184,387</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rate of Consent by Website Visitors</th>
<th>Visitor</th>
<th>Consent Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logged-in visitors (excluding those who consented in person)</td>
<td>23,562</td>
<td>30%</td>
</tr>
</tbody>
</table>

To Date: >14,500 patients enrolled by eIC
Consent for Return of Genetic Results

• Anticipated in informed consent

4. Will I get results of research done using my samples?

• You may receive a newsletter or other information that will tell you about the research discoveries from the Biobank. This newsletter will not identify you or describe any of your personal results.
• Generally, we will not return individual results from research using your samples and data to you or your doctor. Research using your sample is just a stepping stone in learning about health and disease. Most of the findings that come from studying your sample will not be relevant to your personal health. However, in the future, this may change.
• It is important to remember that research results are not always meaningful and are not the same as clinical tests. While you should not expect to receive any results from your participation in this research, if experts from the Biobank decide that research results from your sample are of high medical importance, we will attempt to contact you. In some situations, follow up testing might be needed in a certified clinical lab. You and your medical insurer may be responsible for the costs of these tests and any follow up care, including deductibles and co-payments.
• It is possible that you will never be contacted with individual research findings. This does not mean that you don’t have or won’t develop an important health problem.
• In the future, when research results are published, they may show that certain groups (for example, racial, ethnic, or men/women) have genes that are associated with increased risk of a disease. If this happens, you or others may learn that you are at increased risk of developing a disease or condition.
But then: Biobank Began Genomewide Genotyping

• Had to confront imminent need for operational return of research results
• What to return? Who should confirm? What about genetic counseling?
• How to handle non-CLIA results? How to allow opt-out?
• Privacy issues
• Confidentiality: share with clinicians?
Return of Genetic Results

• Given ongoing, productive relationship with IRB—formed joint task force including Biobank leadership, IRB leadership, medical geneticists, laboratory leadership, genetic counselors
• Process developed over 14 months
• Extended retreat + monthly meetings and interim work
• Consultation with:
  – IRB
  – Office of General Counsel (legal)
  – Genetics services
  – Investigators
  – Community Advisory Panel
  – Partners Academic Executive Committee
• IRB submission => approval: 11 days
Return of Results Workflow

- **Actionable result identified**
  - By investigator or Biobank
  - Review by RoRR Taskforce and Biobank Executive Committee

- **Notified of “research result from your DNA sample that may be important to your health”**
  - Letter, phone, email x 3
  - Letter notes clinical confirmation required
  - Contact Biobank-affiliated GC for discussion

- **Opt-Out**
  - Appointment with GC to discuss finding and next steps
    - GC arranges for new sample tested at LMM at no cost to participant

- **Opt-Out**
  - **Research result not valid**
    - GC addresses participant concerns/questions

- **Opt-Out**
  - **Confirmatory (CLIA) testing. GC notifies participant**
    - Participant choice

- **Option**
  - **Referral to Medical Geneticist**
  - **Share result with participant’s PCP**
    - Provider informed that GC or medical geneticist available for questions/consultation

- **Letter to PCP**
  - Participant informed that:
    - Result will enter EHR
    - Participant responsible for insurance copays/costs of clinical care

- **Result not entered in EHR**
  - By investigator or Biobank
  - Review by RoRR Taskforce and Biobank Executive Committee
Expanding to the *All of Us* Research Program

- Well-prepared for the issues but still challenges in implementation
- Basic, vs. Genomics vs. EHR consent
- Ceding review—local vs. national
- Co-consent with Biobank
  - A lengthy process of debate
  - Operational challenges
    - Minimize participant burden
    - Avoid confusion
    - Institutional policies such as privacy and recruitment
Conclusions

• Implementing IC for genomics in a healthcare system entails multiple challenges (foreseen and unforeseen)

• We have had success by building and sustaining a partnership between investigators and the IRB every step of the way.

• Also essential has been partnering with institutional leadership, clinical staff and our participants (e.g. through our Community Advisory Panel)