The BabySeq Project: Genome Sequencing for Childhood Risk and Newborn Illness

Sarah Kalia, ScM, CGC
Brigham and Women’s Hospital
Harvard Medical School

Project Leadership: Peter J. Park, PhD; Heidi L. Rehm, PhD; Tim W. Yu, MD, PhD; Pankaj B. Agrawal, MD, MMSC; Richard B. Parad, MD, MPH; Ingrid A. Holm, MD, MPH; Amy L. McGuire, JD, PhD; Alan H. Beggs, PhD; Robert C. Green, MD, MPH
Pilot Survey Protocol

(N = 1309)

Approach parents within 72 hours of delivery
Consent parent(s) and randomize family unit to baseline survey

(N = 582)

• Demographics
• Consent to re-contact

(N = 514)

• Demographics
• Consent to re-contact
• Genetics orientation
• Interest in genome screening

3-24 months

(N > 605)

Genetics orientation and randomize to follow-up survey
with or without mock genomic results
How interested would you be in getting genome screening for your baby?

(N = 514)
<table>
<thead>
<tr>
<th>Variable</th>
<th>In-Patient Cohort (n=514)</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± sd (range)</td>
<td>32.7 ± 6.4 (15-65)</td>
<td>1.05 (1.00 – 1.10)</td>
<td>0.066</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>335 (65.2)</td>
<td>1.03 (0.61-1.72)</td>
<td>0.917</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>314 (61.2)</td>
<td>1.53 (0.89 – 2.62)</td>
<td>0.123</td>
</tr>
<tr>
<td>Hispanic or Latino, n (%)</td>
<td>64 (12.5)</td>
<td>0.94 (0.43 – 2.05)</td>
<td>0.882</td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>407 (79.3)</td>
<td>0.36 (0.16 – 0.80)</td>
<td>0.012</td>
</tr>
<tr>
<td>Some graduate school or higher, n (%)</td>
<td>248 (48.3)</td>
<td>0.87 (0.51 – 1.48)</td>
<td>0.611</td>
</tr>
<tr>
<td>First biological child, n (%)</td>
<td>270 (52.7)</td>
<td>1.44 (0.89 – 2.33)</td>
<td>0.142</td>
</tr>
<tr>
<td>Family history of genetic disease, n (%)</td>
<td>70 (13.7)</td>
<td>0.85 (0.42 – 1.73)</td>
<td>0.655</td>
</tr>
<tr>
<td>Infant health concerns, n (%)</td>
<td>29 (5.7)</td>
<td>0.39 (0.16 – 0.91)</td>
<td>0.030</td>
</tr>
</tbody>
</table>
Concordance Analysis

• 168 couples (among 514 parents) rated their interest in newborn genome screening

• 127 couples (76%) reported similar levels of interest

• 41 couples (24%) were discordant in their views
  – Concordance more likely if the couple was married (OR: 2.85, p=0.012)
Limitations

• Participants rated their hypothetical interest. Actual uptake was not measured.

• Mothers and fathers queried around the same time, perhaps influencing responses.

• Increased anxiety or confusion about NBS was not tracked.
The BabySeq Project
(U19 HD077671)

• First randomized trial to explore benefits and risks of genome sequencing (GS) in healthy and sick newborns
• 240 healthy newborns
• 240 NICU newborns
• Parents and physicians
• Timeline: 2013-2018
Pre-Enrollment Genetic Counseling, Consent, Blood Draw, Family History with Genetic Counselor

240 Healthy Newborns at BWH and Parents
• Standard of Care NBS
• Family History

240 Newborns in NICU at BCH and Parents
• Standard of Care NBS
• Family History
• Genome Report

Optional:
• Indication-Based Report

Consultation and Results Disclosure with Genetic Counselor and Study Physician. Consultation Note and Testing Reports placed in Medical Record and sent to other care providers

10-month Follow-up Appointment and Exam with Study Physician and Genetic Counselor

Medical Record Review
Workflow for Infant and Parents

Healthy infant born at BWH or BCH NICU admission eligible for study

RA approaches parents, provides study info

Pre-Enrollment Genetic Counseling, Consent and Baseline Visit/Survey

Results Disclosure Visit/Survey

1-Week Post-Disclosure Phone Call

3-Month Post-Disclosure Survey

10-Month Post-Disclosure Visit/Exam/Survey

Study Physicians and Genetic Counselors available for Qs
Neonatologists, NICU Specialists, Community Pediatricians receive Baseline/Attitudes Survey (completion = consent)

- None of MD’s patients enroll
  - Baseline Survey reminder if incomplete
  - Receive summary of results disclosure by study GC to family. Option to discuss with study GC/MD
  - Post-Disclosure/Utilization Survey (completion = consent)
  - End of Study/Attitudes Survey (completion = consent)

- MD’s patient(s) enroll, randomized to NBS-only
  - Baseline Survey reminder if incomplete
  - Receive summary of results disclosure by study GC to family. Option to discuss with study GC/MD
  - Post-Disclosure/Utilization Survey (completion = consent)
  - End of Study/Attitudes Survey (completion = consent)

- MD’s patient(s) enroll, at least 1 randomized to GS+NBS
  - Baseline Survey reminder if incomplete
  - Receive summary of results disclosure by study GC to family. Option to discuss with study GC/MD
  - Post-Disclosure/Utilization Survey (completion = consent)
  - End of Study/Attitudes Survey (completion = consent)
## Data Collection Domains

<table>
<thead>
<tr>
<th>Survey Domain</th>
<th>Parents</th>
<th>MDs</th>
<th>Parents</th>
<th>MDs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Post-Disclosure</td>
<td>3 month Follow-up</td>
<td>10 month Follow-up</td>
</tr>
<tr>
<td>Attitudes</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived Utility</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Healthcare Utilization</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Health Behaviors &amp; Intentions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent-Child Relationship</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceptions of Child</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal Distress</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partner Relationship</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The BabySeq Project Team

Leadership
Alan H. Beggs, PhD (Joint PI)
Robert C. Green, MD, MPH (Joint PI)
Peter J. Park, PhD
Heidi L. Rehm, PhD
Tim W. Yu, MD, PhD
Pankaj B. Agrawal, MD, MMSC
Richard B. Parad, MD, MPH
Ingrid A. Holm, MD, MPH
Amy L. McGuire, JD, PhD

Co-Investigators, continued
Harvey Levy, MD
Philip Lupo, PhD, MPH
David Miller, MD, PhD
Patrice Milos, PhD
Ann Poduri, MD
Steve Ringer, MD, PhD
Amy Roberts, MD
Jason Vassy, MD, MPH
Susan Waisbren, PhD
Louise Wilkins-Haug, MD, PhD

Co-Investigators
Ozge Ceyhan Birsoy, PhD
Kurt Christensen, PhD
Leslie Frankel, PhD
Anne Hansen, MD, MPH
Lise Johnson, MD
Joel Krier, MD
Bill Lane, MD, PhD

Consultants
George Church, PhD
Lisa Diller, MD
Dmitry Dukhovny, MD, MPH
Steve Joffe, MD, MPH
Peter Kraft, PhD
Michelle Lewis, MD, JD
David Margulies, MD, PhD
Neela Sahai, MD

Advisory Board
Bruce Korf, MD, PhD (Chair)
Les Biesecker, MD
Steve Cederbaum, MD
Alex Kemper, MD, MPH
Zak Kohane, MD, PhD
Lou Kunkel, PhD
Jim Lupski, MD, PhD
Sharon Terry, MA
Chris Walsh, MD, PhD

Staff
Lily Hoffman-Andrews
Ali Noorbaksh
Stacey Pereira, PhD
Jill Robinson, MA
Rebecca Walsh

Special thanks to
Danielle Bäck
for contributing slides
Thank You

Questions?
Comments?

skalia@genetics.med.harvard.edu