Early Check – A Newborn Screening Research Program in North Carolina

November 9, 2023

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RTI International
Disclosures

Early Check is supported by:

- The Leona M. and Harry B. Helmsley Charitable Trust
- JDRF International
- Janssen Pharmaceuticals
- Travere Therapeutics
- Orchard Therapeutics
- Sarepta Therapeutics
- Muscular Dystrophy Association

Laboratory Partners

- GeneDx
- Illumina
Agenda

• Early Check study
• Addition of genomic sequencing and T1D genetic risk scores
• How are the lessons learned from the first 5 years of Early Check informing risk for T1D screening?
• Early data
Early Check: A Voluntary Newborn Screening Program

Screening newborns in N.C. since 2018

Research Triangle study may help save children's lives

WRAL
June 2021

Early Check Panel

- Duchenne Muscular Dystrophy (DMD) and related conditions
- Fragile X Syndrome (FXS)
- Spinal Muscular Atrophy (SMA)

Welcome to Early Check! Let's get started.
Early Check is a research study that checks for two rare but serious health problems in newborns. The screening tests are free.
Parents can sign up when pregnant or within 4 weeks after the baby is born.
Watch this short video to learn about
Objective: Respond to opportunities facing newborn screening

- Genome (and ‘Omic’) technologies
- Precision medicine advances, including for common disorders
- Rapidly growing pipeline of transformative therapies
Sequencing study aims (initial 3-year study with plans to continue)

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>Implement and evaluate the use of genome sequencing (GS) to screen up to 10,000 newborns for childhood-onset, monogenic conditions.</td>
</tr>
<tr>
<td>2</td>
<td>Determine uptake and acceptability of GS newborn screening among parents of eligible newborns.</td>
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<tr>
<td>3</td>
<td>Implement and evaluate short-term follow-up procedures to inform public health application.</td>
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<tr>
<td>4</td>
<td>Assess 12-month outcomes for children with positive results and their caregivers.</td>
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</table>
Type 1 diabetes aims (initial 3-year study with plans to continue)

1. Conduct formative research among parents, primary care providers, specialists, and public health professionals on using genetic risk scores in newborn screening for type 1 diabetes.

2. Prepare for, implement, and evaluate a pilot study to screen at least 5,000 newborns for increased risk for type 1 diabetes.

3. Determine uptake and acceptability of type 1 diabetes screening among parents of eligible newborns, compared with outcomes from panels of rare monogenic conditions.

4. Assess 12-month outcomes for children with increased risk for type 1 diabetes and their caregivers.
## Early Check Panel

<table>
<thead>
<tr>
<th>Treatable Conditions (~180)</th>
<th>Conditions with Potential Treatments (~30)</th>
<th>Risk for Type 1 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinoblastoma</td>
<td>Duchenne muscular dystrophy</td>
<td></td>
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<tr>
<td>Neonatal diabetes</td>
<td>Menkes disease</td>
<td></td>
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<tr>
<td>Hemophilia</td>
<td></td>
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<tr>
<td>Fructose intolerance</td>
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</table>
The first 5 years informing Early Check’s future

We can screen thousands of infants per year with a very low touch approach and no study visit.

State partnership is essential for large-scale screening to inform public health.

User-centered electronic informed consent can successfully support a low-touch informed choice.

Electronic return of results can be successful, facilitating large sample sizes.
Process Overview

RECRUITMENT
MULTI-PHASE PUBLIC OUTREACH

PERMISSION
PARENTS CHOOSE TO SIGN UP AND WHICH TESTS ONLINE

SCREENING TEST
GENOMIC SEQUENCING

FOLLOW-UP
ASSESSMENTS, SUPPORT, AND INFORMATION

T1D RISK RESULT
RETURNED IN PORTAL

POSITIVE MONOGENIC RESULT
RETURNED BY GENETIC COUNSELOR

NEGATIVE MONOGENIC RESULT
RETURNED IN PORTAL

DIAGNOSIS
CARE COORDINATION AND GENETIC COUNSELING

FOLLOW-UP TESTING

SURVEY PARENTS
Obtain Consent in the Portal

What does Early Check Screen For?

Early Check offers screening for hundreds of serious rare health conditions and also checks the risk for type 1 diabetes.

Parents can choose which types of health conditions they want screened for their baby. To help you decide, we put these screening tests into three groups.

Here are brief descriptions of the Early Check screening groups:

- **Group 1 - Treatable Conditions**
- **Group 2 Optional - Conditions with Potential Treatments**
- **Group 3 Optional - Risk for Type 1 Diabetes (T1D)**

**Group 3 Optional – Risk for Type 1 Diabetes (T1D)**

- Early Check will check your baby’s DNA to learn the genetic risk for Type 1 Diabetes, a fairly common and treatable health condition.
- T1D is the most common form of diabetes in children. Babies are not born with T1D, but it can show up later in childhood. Testing can provide information about your child’s risk for T1D.
- Type 1 Diabetes (T1D) causes children to have serious symptoms or die if not treated.

**Why is this information important?**

- Knowing if your baby has a higher risk for T1D lets parents watch for signs of the condition. This could lead to earlier diagnosis, treatment and better health for a child with T1D.
Obtain Consent in the Portal

Which screening groups do you want to learn more about?

All babies signed up for Early Check get testing for the Treatable Conditions (Group 1).

Conditions with Potential Treatments (Group 2) and Risk for Type 1 Diabetes (Group 3) are optional screening groups.

Select the optional groups below to read more about screening for these health conditions.

Then click the “Next” button to move on to the next screen.
Video: How is Early Check screening done?
T1D GRS screening

- Public health unprepared for screening or follow-up if GRS results were included in newborn screening
- Model screening in a public health-like setting
## T1D Screening Process Overview

<table>
<thead>
<tr>
<th>RTI</th>
<th>Laboratory Partner</th>
<th>RTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Obtain consent in portal</td>
<td>• DNA extraction</td>
<td>• Extract SNPs from genome data</td>
</tr>
<tr>
<td>• Match consent to dried blood spot (DBS) specimens at state lab</td>
<td>• Genome sequencing</td>
<td>• GRS2’ calculation</td>
</tr>
<tr>
<td>• Obtain punches from DBS card</td>
<td>• Prepare genome data and send to RTI</td>
<td>• Genetic similarity to determine which ancestry thresholds to use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Results reported in portal</td>
</tr>
</tbody>
</table>

Consent portal opened for enrollment on September 28th
Return of Results in the Portal

<table>
<thead>
<tr>
<th>Group</th>
<th>T1D risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low concern</td>
<td>&lt;2%</td>
</tr>
<tr>
<td>Moderate concern</td>
<td>&gt; 2 to &lt;5%</td>
</tr>
<tr>
<td>Higher concern</td>
<td>&gt; 5 to 10%</td>
</tr>
<tr>
<td></td>
<td>&gt; 10%</td>
</tr>
</tbody>
</table>

Welcome back, Angela! We're glad you're checking in.

<table>
<thead>
<tr>
<th>Test</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>HISTORICAL EARLY CHECK</td>
<td>Mar 20, 2020</td>
</tr>
<tr>
<td>GROUP 1</td>
<td>Aug 15, 2023</td>
</tr>
<tr>
<td>GROUP 2</td>
<td>Aug 15, 2023</td>
</tr>
<tr>
<td>T1D</td>
<td>PENDING</td>
</tr>
</tbody>
</table>

Questions?
Whether you signed up for Early Check 4 hours ago or 4 months ago, you might have some questions. See Answers to Frequently Asked Questions or here at Contact Us.
Return of Results in the Portal

What’s my baby’s result?

**Higher Concern** for Type 1 Diabetes (T1D): Act

Based on the Early Check DNA testing, your baby’s risk for getting type 1 diabetes later on is higher than most. Most babies with this result will not get T1D, but some will.

Early Check recommends additional testing.

- **Low concern**: AWARE
  - Less than 2% risk for T1D in the future

- **Moderate concern**: WATCH
  - 2% - 5% risk for T1D in the future

- **Higher concern**: ACT
  - 5% - 10% risk for T1D in the future
For babies with this Higher Concern result, what is the risk for getting type 1 diabetes during their lifetime?

Risk for type 1 diabetes during their lifetime

Your baby may be more likely to get T1D than usual. 5%-10% of babies with this result will develop type 1 diabetes during their lifetime.

Here are some things to know:
- TID usually starts in childhood.
- Sometimes it doesn't start until adulthood.
- Signs of TID are rare in the first year of life.
T1D Follow-up

Screen newborn for T1D
DBS -> genome sequencing -> GRS calculation

Low concern & Moderate concern

Return of results and parental education through the Early Check portal
Parental education via group video visit offered at 4-6 months
Education and resources provided by email yearly

Higher concern

Return of results and parental education through the Early Check portal
Autoantibody testing at 9 months
Baby tests negative for autoantibodies

Parents express concerns about baby’s health or significant anxiety about results

Baby tests positive for 1 or more autoantibody
Second autoantibody test at 12 month
Baby tests positive for 1 or more autoantibody

Inform and educate pediatrician with parent approval

Study visit with UNC pediatric endocrinologist

*Moderate concern plus first degree relative w/ T1D receives higher concern follow-up
Initial Enrollment Data

- Goal: Screen 5,000+ babies for monogenic panels and T1D GRS
- Enrollment opened 9/28/23
- ~95 babies screen/week
- Initial screening results expected early December

<table>
<thead>
<tr>
<th></th>
<th>Everyone</th>
<th>T1D Selected</th>
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</thead>
<tbody>
<tr>
<td>Babies enrolled</td>
<td>239</td>
<td>175</td>
</tr>
<tr>
<td>100%</td>
<td>73%</td>
<td></td>
</tr>
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Early Check – A Newborn Screening Program in North Carolina
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<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td><strong>Babies</strong></td>
<td>239</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Mom's Race/Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>153</td>
<td>64.0%</td>
</tr>
<tr>
<td>Hispanic/Latino or Spanish</td>
<td>25</td>
<td>10.5%</td>
</tr>
<tr>
<td>Asian</td>
<td>22</td>
<td>9.2%</td>
</tr>
<tr>
<td>African American/Black</td>
<td>16</td>
<td>6.7%</td>
</tr>
<tr>
<td>Hispanic/Latino or Spanish,White</td>
<td>5</td>
<td>2.1%</td>
</tr>
<tr>
<td>Prefer not to respond</td>
<td>5</td>
<td>2.1%</td>
</tr>
<tr>
<td>African American/Black,White</td>
<td>4</td>
<td>1.7%</td>
</tr>
<tr>
<td>American Indian/Alaskan Native,White</td>
<td>2</td>
<td>0.8%</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Middle Eastern/North African</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>None fully describe me</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Asian,White</td>
<td>1</td>
<td>0.4%</td>
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<tr>
<td>American Indian/Alaskan Native,Asian,Hispanic/Latino or Spanish,White</td>
<td>1</td>
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<td><strong>Dad’s Race/Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>156</td>
<td>65.3%</td>
<td>124</td>
<td>70.9%</td>
</tr>
<tr>
<td>Hispanic/Latino or Spanish</td>
<td>30</td>
<td>12.6%</td>
<td>23</td>
<td>13.1%</td>
</tr>
<tr>
<td>African American/Black</td>
<td>20</td>
<td>8.4%</td>
<td>12</td>
<td>6.9%</td>
</tr>
<tr>
<td>Asian</td>
<td>17</td>
<td>7.1%</td>
<td>9</td>
<td>5.1%</td>
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</tr>
<tr>
<td>African American/Black,White</td>
<td>3</td>
<td>1.3%</td>
<td>0</td>
<td>0.0%</td>
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<td>1</td>
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<td>Middle Eastern/North African,White</td>
<td>2</td>
<td>0.8%</td>
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<td>1</td>
<td>0.4%</td>
<td>1</td>
<td>0.6%</td>
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Early Check Sequencing Leadership Team

Holly Peay
Project Director

Heidi Cope
Associate Project Director

Lisa Gehtland
Administrative Core Lead

Don Bailey
Senior Advisor

Don Bailey
Senior Advisor

Cynthia Powell
UNC PI, Geneticist

Liz Jalazo
Geneticist

Anne Wheeler
Follow Up Core Lead

Melissa Raspa
Methodology Core Lead

Kate Kucera
Lab Core Lead

Jonathan Berg
Geneticist

Jennifer Law
Endocrinologist

RTI International

UNC Chapel Hill

Scott Shone,
NCSLPH PI

NC State Laboratory of Public Health
Thank you

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