SAVING BABIES?

THE CONSEQUENCES OF NEWBORN GENETIC SCREENING

Stefan Timmermans and Mara Buchbinder

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Fieldwork Encounters and Discoveries

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TO JESSE
AND JASPER

Contents

Acknowledgments

Imagine a screening program performed at birth for very rare conditions. The rationale for the program is prevention: early detection promises to save babies from a sudden death. Sound appealing? Now, add that medical scientists did not know much about the conditions being screened, that it is not actually that easy to diagnose an infant based on screening results, and that the link between screening and preventive treatment is not clear. Even after a disorder is picked up with screening, some infants will still develop complications and others will die as a result of the disorder. Still, the program is state-mandated and in most locations does not require informed consent: parents are presumed to agree with screening unless they opt out. Clinicians cannot ignore the results either, because the state requires them to follow up with parents. To further complicate the issue, let's locate this screening program in a country known for persistent health inequities—a country where access to care and the quality of care remain overdetermined by market forces and a country that persistently trails behind other industrialized nations in comparative health indicators. A country, in short, in which a positive screen does not automatically mean access to care.

This country, of course, is the United States and the program is universal newborn screening. This program expanded in 2005 to screen virtually all newborns in the United States for more than 50 rare genetic conditions. This book examines how newborn screening was expanded and how families and clinicians experienced positive newborn screens in the aftermath of this expansion. Out of all of the possible health services that could have been made universally available, why did US health policymakers opt for expanding newborn screening? How do parents and clinicians act upon a positive screen when the results remain uncertain? In

what follows, we examine the intended and unintended consequences of the expansion of newborn screening.

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Introduction

The Consequences of Newborn Screening

Holding up a $20 bill dramatically at a 2008 press conference, model and actress Renee Baio demonstrated the cost of screening a newborn baby for rare genetic conditions to the gathered journalists. With her husband, actor and director Scott Baio—best known for his role as Chachi Arcola on the TV sitcom *Happy Days*—Renee Baio had founded the Bailey Baio Angel Foundation to promote the expansion of newborn screening in the United States and to provide support for families of children diagnosed with organic acidemia oxidation disorders.[1] The organization was named after their daughter Bailey, who screened positive for glutaric acidemia type 1 (GA1) at birth. People with this condition cannot metabolize the amino acids lysine, hydroxylysine, and tryptophan and accumulate one or more toxic metabolites in their blood. The accumulation of these metabolites can lead to a metabolic crisis, an illness episode marked by vomiting, lethargy, difficulty feeding, and irritability that can result in brain damage, coma, or even death. Even without such a crisis, GA1 patients may experience developmental delays, poor growth, and muscle spasticity. Although there is variation in the symptomatic manifestation of the condition, geneticists consider it a very serious disease.

The Baios had called this press conference to urge legislators to adopt expanded newborn screening. The United States has had a newborn screening program in place since the 1960s but, as is typical for US healthcare, individual states determine which conditions to screen for. Between 1970 and 2000 great discrepancies developed, with some states screening for 3 conditions while others screened for up to 36 conditions. In 2006, the American College of Medical Genetics issued a report calling all states to

screen for 54 conditions.[2] These recommendations were championed by several advocacy organizations—including the March of Dimes and the parent advocacy organization Save Babies Through Screening Foundation, Inc., with whom the Baios later joined forces.

The rationale for expanding newborn screening is powerful. The appeal resides in secondary prevention. Rather than treating children with devastating metabolic conditions, screening advocates hope to forestall the onset of symptoms. Newborn screening identifies infants who have a condition but are still asymptomatic and offers them preventive measures that may postpone symptom development.[3]

Strangely, however, the Baios' encounter with newborn screening did not fit this public health rationale. We interviewed Renee and Scott Baio about their own experience with newborn screening in 2009, 20 months after Bailey's birth.[4] When we arrived at their house, Bailey welcomed us, clutching a SpongeBob SquarePants doll. Sitting in their glass-enclosed breakfast room, Scott and Renee explained how they "went through hell" during the first 10 weeks of Bailey's life. Accustomed to talking to journalists,[5] they told us their story without much prompting. The couple had been dating for about two years when Renee found out she was pregnant, the day after Scott's father passed away. Scott was 45 and Renee was in her early thirties. They married when Renee was six months pregnant.

In the 11th week of her pregnancy, Renee started to bleed. An ultrasound showed that she was pregnant with twins. Several days later, however, she lost one of the fetuses. She recalled, "I go back to the hospital because I'm still spotting two or three days later and there just starts to be a mass of blood. It's a small mass of blood and then as one sac's getting smaller, the mass of blood is getting bigger. And then there was no second heartbeat. It just dissolved itself. I passed one and kept the other." Renee stayed on bed rest for a few weeks until she entered the second trimester. She explained that losing the twin "was very emotional. As a mother you want to know why. Why did you lose this baby; why?" Scott added: "I didn't know which end was up. She's telling me we're having twins and I'm just sort of getting over the fact that my father died and we just miscarried a baby." Renee recalled that Scott was not emotional during the pregnancy "until he laid eyes on [Bailey] and then it was instant change." This turnaround did not last long.

On day five of Bailey's life, the Baios received a phone message instructing them to visit their pediatrician's office to repeat a blood test. Bailey "tested positive for something" but the pediatrician refused to say

what it was. A nurse from the state newborn screening program followed up several days later with a phone call to make sure that they had retested the baby. Playing dumb, Renee said she wasn't sure how to spell the name of the condition. The nurse spelled g-l-u-t-a-r-i-c a-c-i-d-e-m-i-a type 1. Renee had previously researched phenylketonuria (PKU) because that was, at the time, the most common metabolic condition identified through newborn screening. The name glutaric acidemia did not ring a bell. Scott and Renee confronted their pediatrician with the diagnosis and asked her whether it was worse than PKU. The pediatrician said that she wished the nurse had not told her the name of the condition because they would discover the worst-case scenario on the Internet. She admitted that "yes, it was worse than PKU," but she also added that the diagnosis was not firm yet.

The news took a toll on the recently created family. Renee recalled that Scott "was afraid to bond with [Bailey] once we got the positive [screening result]." Scott agreed that he "had a hard time." Renee recalled, "He did not want to hold Bailey." Scott explained, "Because I thought she was going to die. And then I didn't want to open my heart up and get completely crushed for the rest of my life." The positive result also caused tension in their marital relationship. Renee said, "My family lives in Tennessee. So of course, this is their grandchild. They want to know what's going on. I had her five weeks early—emergency C-section. They weren't here for that. And they're calling me. They want know what's going on and now they're concerned. So I wasn't allowed to have him hear me talk on the phone or he would bust in to the baby's room and he would say, 'She effing has it.' It was a rage, is what it was. I think I was on the verge of a nervous breakdown because here I'm trying to nurse this baby and bond with this baby." She added, "I thought for sure if she had it I would be a single parent."

For 10 excruciatingly long weeks, Renee and Scott waited for the results of a skin biopsy that would determine whether Bailey had GA1. Bailey's newborn screen value for glutarylcarnitine (C5DC), the biological marker for GA1, was 0.35 μmol/L, which was the cutoff point for GA1 at the time. With other conditions, newborn screening program officials might have wavered over whether to contact the parents about values lying at the cutoff point, but because GA1 is considered such a serious condition, the geneticists initiated follow-up testing. They specifically retested blood plasma and urine for C5DC, and again, the blood levels were slightly elevated. The next step was to do a skin biopsy and test for the genetic mutations implicated in GA1. However, only one laboratory in the

country processed these biopsies and because the sample was taken right before the Thanksgiving holiday, the sample was not even sent there for two weeks. The Baios waited anxiously. Their geneticist tried to reassure them based on Bailey's apparent normal development but Scott wanted a clean bill of health based on genetic results.

Renee was prepared to put everything on hold until Bailey was out of the danger zone: "I was physically ready to hunker down in that baby's room for six years. Because the geneticist said that if you can get through the first six years without any metabolic crises, no fever, no vomiting, then you have somewhat of a chance. I was ready. I was ready to have everyone wear masks when they come in. I would just hunker and keep her in that room for six years. And me not leave. That's what I was ready to do." The couple started a crash course about GA1, requesting dietary supplements that could prevent symptom development. Renee explained: "All of it was tough. It was tough going for me to get the special formula downtown. It was tough for me to go the pharmacy to get the compound. It was so hard to go get it because every time I would go get it, it was a reaffirmation that my kid might be sick."

Renee attributed her decision to stop breastfeeding at six weeks to the stress of not knowing. At that time, the pediatrician suggested treating Bailey for "failure to thrive" because she wasn't gaining sufficient weight. The treatment involved supplementing Bailey's diet with extra protein, which could exacerbate the GA1 if Bailey did indeed have it. Renee reflected on the options she faced: "Okay my kid is going to be failure to thrive and she's either going to starve to death or we have to give her protein and I could be potentially causing my child brain damage." She felt she had failed as a mother.

Finally, in January 2008, the results came in. Renee recalled:

> We had an appointment for Monday, January 13th. I told the nurse, "If the tests come in, I don't care if it's a Wednesday, Thursday, Friday; please just tell us. Just call me on the phone. Call me. Call me. Call me." I begged her and I'm calling her sometimes twice a day. Then on that Friday, January 11th, there was a celebrity baby gifting suite over in Beverly Hills. We decided to go because we went through her first Thanksgiving, her first Christmas, our wedding and everything was just kind of—we were numb. And so Scott said, "Let's go," because we knew that that Monday was our D-Day. So he said, "Let's just go and let's just try to enjoy it." We went through all the motions and got the free baby gifting things. While we were there, I got the phone call, but I didn't hear

> my cell phone ring. We're in the valet and I'm like, "Oh my God." So I tried to call my voice mail and that's the one day that T-Mobile was upgrading their voice mail. We get home and they had left a message on the home phone. I tried to call the voice mail box here at the house and just as she's getting ready to tell me, she goes, "Hi, this is Carla from newborn screening." The phone went dead because it had been off the charger. So I've gotta run to the other end of the house and Scott and my older daughter are like, "What'd they say? What'd they say?" So I had to run to the other end of the house to get the other phone, run back to the baby's room and they said, "Hi, this is Carla from newborn screening. I just want to let you know that it was a false positive and your baby is fine." And then I hit the floor.

At the time of our interview, the Baios' relationship was still recovering from this near brush with disease. Renee reflected: "We went from a relationship of two years of never arguing, never having any type of friction between us, nothing negative really ever. Maybe about the dog being in the kitchen or just small stuff. But it went from that to totally living together, him losing his father, me pregnant and losing a baby. And then we've got this baby that's potentially sick. It was just boom, boom. We're still trying to climb out of it. It almost ruined our marriage."

The experience with newborn screening galvanized the Baios to start a charitable foundation. Scott had pledged that if his daughter did not have glutaric acidemia, he would devote his energy to setting up a foundation for children with the disorder: "It's like an underground disorder. A lot of people don't know about it, they've never heard about it. A lot of people don't know when they bring their baby home what the heel stick is for."

* * *

The Baios' experience goes to the heart of this book. From a public health or medical perspective their ordeal does not count for much: Bailey's case was included in a state database of false positives and this measure represents the only official record of her screening experience.

What is medically invisible ends up being deeply meaningful socially, however. The encounter with newborn screening shaped Scott and Renee's young marriage, their charitable work, and their relationship with their daughter. The Baios are unique in their ability to leverage their celebrity status to create a charity complete with publicists and easy access to the press. Their experience is more typical, however, in how their daugh-

ter's newborn screening results came as a deep shock, how their baby did not show any symptoms but might have harbored a life-threatening condition, how they lived in suspense for months before finding out whether their child had a disease, how they were willing to go to great lengths to do the best for their child, how they treated something that ended up being a nondisease as a disease for a short period of time, and how even though Bailey had been cleared of disease, some lingering questions about her elevated levels remained.

If the Baios' harrowing experience does not register in the official program statistics, what narratives drive newborn screening policy? The common approach in medical and advocacy circles is to tell the story of the scientists who made newborn screening possible and to focus on dramatic patient stories as indicators of medical salvation. In fact, that is how the Baios talk publicly about newborn screening. Every month, their foundation website highlights an "angel," a child diagnosed with an organic acidemia disorder. Scott and Renee report heart-wrenching stories about infants with devastating conditions who had the misfortune of being born in states that did not screen for these conditions. If only they had been born in a neighboring state, the message goes, these children might have been saved. This is an emotionally powerful narrative that forms a benchmark for evaluating the efficacy of newborn screening. But it is not the only narrative. The Baios' own experience does not, in fact, fit in. Renee and Scott are careful not to present themselves as the face of organic acidemia disorders because, in the end, their daughter was not diagnosed with one.

In this book, we will highlight a fuller spectrum of effects that newborn screening has created for families and clinicians. We do not make the case for or against newborn screening. If anything, we found strong support for screening. The Baios' channeling of a difficult experience into pro-screening activism is telling of the appeal of newborn screening. All parents in our study, regardless of the final outcome, remained steadfast in their support of the screening program, although some would have preferred a different communication process or more supportive services.

We happened to be in the right place at the right time to observe newborn screening unfolding. In California, the setting of our research, expanded newborn screening had only been in place for about two years when we began our study in November 2007. This is how the process works. The state Department of Public Health ensures that every baby born in California receives a heel prick to collect a small amount of blood between 24 hours and six days after a baby's birth. Babies born at home without

medical supervision are tracked through the county registrar to make sure that they receive the screen. The birth registrar provides the parents with an informational brochure that explains how to get their infant screened, and also informs the newborn screening program of any births that occur outside hospital facilities. The program is able to screen 99 percent of the 1,500 babies born in California each day with only 1 percent inadequate samples.[6] The California experience is typical for the United States: currently, more than 99 percent of the more than four million newborns born annually are screened for more than 50 rare genetic conditions.[7]

Newborn screening is de facto mandatory because parental consent is not required except for in the District of Columbia and two US states: Maryland and Wyoming.[8] Parents in 30 states, including California, can opt out of screening for religious reasons, and in 13 states parents can opt out for any reason.[9] The default position, however, is to screen every newborn. In fact, one state without religious exemption has removed a child from parental custody to conduct newborn screening.[10] Hospital personnel present the heel prick as a routine matter during the hospital checkout procedures, along with other bureaucratic forms and handouts about feeding and well-baby visits.

Typically, a nurse will stab the child's heel with a sharp triangular-shaped piece of metal. The nurse squeezes the heel until a drop of blood forms. The first drop is wiped away and the second drop is blotted upon a special card. These cards are sent to state laboratories to be processed. Most parents never hear from the newborn screening program because the blood sample screens negative. In those cases, the newborn screening program sends the screening results to the hospital and the physician listed on the screening form, usually a primary care physician or pediatrician.

If a blood sample screens positive for a target condition, the results are followed up through a network of clinical care coordinators that work for the state newborn screening program. (Note that "positive" refers to a result that lies outside of a predetermined normal range: the value is either higher or lower than that of the average infant.) First, the clinical care coordinator will contact the child's primary care provider to ask for a follow-up test. If no physician is listed on the birth certificate, coordinators rely on a network of state public health nurses to track the family down. The physician's office calls the parents and schedules the follow-up test: a confirmatory blood test, and often a urinalysis, depending on the condition. In the majority of the retested cases, the follow-up test is negative and the physician is informed that there is nothing to worry about. If

the values still remain positive, the clinical care coordinator refers the patient to a regional specialty follow-up center under contract with the state, where a member of the clinical staff schedules a clinic visit to conduct additional tests and, if necessary, initiate treatment.

This is where we came in. This book draws on our ethnographic research in one specialty follow-up center in California. The clinic we studied specializes in the treatment of children's metabolic disorders.[11] For nearly three years, we followed 75 families whose children's newborn screening results lay outside of a preset normal range. We attended the weekly outpatient clinic, observed and recorded consultations between geneticists and families, sat in on staff meetings, and examined patients' medical charts. We also interviewed clinicians, parents, and policy actors about their experiences with newborn screening. This book tracks the intended and unintended consequences of expanded newborn screening for clinicians and families, both in and out of the clinic.

How to Study Newborn Screening?

Proponents of expanded newborn screening have imbued newborn screening with tremendous potential for benefits. Take this quote from the influential American College of Medical Genetics report that helped to catalyze the expansion:

> States and territories mandate newborn screening of all infants born within their jurisdiction for creating treatable conditions that may not otherwise be detected before developmental disability or death occurs. Newborns with these disorders typically appear normal at birth. The testing and follow-up services of newborn screening programs are designed to provide early diagnosis and treatment before significant, irreversible damage occurs. Appropriate compliance with the medical management prescribed can allow most affected newborns to develop normally. . . . As the model for public health-based population genetic screening, newborn screening is nationally recognized as an essential program that aims to ensure the best outcome for the nation's newborn population.[12]

With every phrase in this passage, newborn screening is enriched with benefit potential. The goal is the prevention of "developmental disability or death" and "significant, irreversible damage." The mechanism of "early diagnosis and treatment" followed by "appropriate compliance with the medical management" leads to the promise that "most" infants "develop

normally." Four additional elements are key. First, *hidden danger*, meaning that without newborn screening no one would suspect that the infants were at risk: "newborns with these disorders typically appear normal at birth." Secondly, *urgency*: "early" intervention is necessary. Thirdly, *universality*: as a "public health-based population genetic screening" program, all infants should be screened. And finally, "testing and follow-up" suggests that screening by itself is insufficient but a *lifelong, integrative, systemic approach* is required to achieve health benefits.

When we compare this account with the Baios' experience, we find that the policy logic of secondary prevention does not adequately capture the multiple meanings that newborn screening held for the family after hearing that Bailey was flagged with a possible disorder. The danger of losing Bailey when she looked and behaved fine affected every aspect of the Baios' relationship as a recently married couple and a newly constituted family. Scott indicated, "I didn't want to open my heart up and get completely crushed for the rest of my life."[13] Although both parents were willing to put their lives on hold to save Bailey, they were not sure that their relationship would survive the bout with a serious metabolic disorder. A positive newborn screen thus triggered a broad array of actions, only some of which fall under the intended goal of prevention.

Prevention did not fully explain the work of clinicians, either. While the policy logic of secondary prevention is oriented toward population outcomes, the job of clinicians is both more mundane and more complex because they respond to individual patients in the here and now. This means that sometimes they aim to prevent the onset of disease, other times they try to talk parents out of going overboard with preventive measures, and on still other occasions they face the difficult task of communicating that prevention is not going to save a baby.

After witnessing our first encounters between parents and clinicians, we realized that policy visions do a poor job of capturing the effects of newborn screening in the clinic. Prevention is too limited and too vague a framework to explain the clinical outcomes of newborn screening: it is only one possible outcome at the end of a lengthy trajectory. Our approach in this book is to examine the broad range of intended and unintended consequences and the daily effects of screening as they unfolded in the clinic. We follow how people act and react, and if these actions prevent the onset of diseases, we are interested in the specific kind of prevention that newborn screening achieves in the lives of infants and its effects on the larger healthcare field.

Here, we are on the lookout for the *consequences* of newborn screening,

an approach drawn from pragmatist theory. These consequences include the ability of newborn screening results to produce emotions, prompt courses of action, suggest justifications, revise previous understandings of disease, and make dietary decisions reasonable. This means that we do not presume to know what newborn screening is and then track its impact on people's lives. Rather, it is through its practical consequences that newborn screening exists and is imbued with specific meanings. *Newborn screening is what it does*. We are interested in the practical difference newborn screening makes: what is the added value you obtain from a positive screen? Actions and experiences are the concrete imprints of the impact of newborn screening that constitute what newborn screening is about.

One implication of this approach is that we take a broad perspective on relevant consequences. Newborn screening technologies connect the biological body at the molecular and symptomatic level with macro factors such as the third-party payer health insurance system in the United States. Screening and test results, possible symptoms of developmental delay, and metabolic crises are not inevitable, predictable, or well-understood entities: they become opportunities for further interpretive actions. In turn, regulatory actions to reimburse dietary supplements directly affect both bodily processes and opportunities for medically sanctioned action. In fact, the micro and macro, the social and physiological converge. We do not decide a priori which consequences are salient, but instead follow the impact of newborn screening wherever it may lead.

Situations of friction, in which habitual ways of thinking and doing no longer seem to work, are of particular interest because they call for improvisation and innovation. Such anomalous situations invoke what the pragmatist philosopher Charles S. Peirce called *abduction*, an inferential creative process that produces new hypotheses and modes of action. For Peirce, people constantly perform abduction in their everyday life, continuously recalibrating their expectations of the future when they face surprising phenomena. We put a child to bed, hear a loud "boink" noise, followed by crying, and presume that the child fell out of bed. In everyday life as in science, such conjectural hunches require corroboration with further evidence. Peirce distinguished two kinds of surprise: novelty, or a new experience, and anomaly, or an unexpected experience. Peirce conceptualized the process of abduction as both a logical inference and a flash of insight occurring when one's mind wanders.[14] We do not need to follow Peirce's speculation about the cognitive foundation of insight. Indeed, a more sociological approach would attend to the cultural schema

and available resources that make such flashes of insight more likely.[15] Healthcare providers and parents facing puzzling clinical situations have developed transposable problem-solving repertoires.[16] Abductive insights prompt a process of trial and error to verify one's hunches that may result in new knowledge about disease, new patient categories, and new modes of managing patients. The unexpected, creative consequences of expanding newborn screening drive our analysis.

A focus on the creative potential of consequences does not imply a naïve inductivism in which the meanings of newborn screening emerge continuously de novo out of an experiential flow. Clinics, healthcare systems, and families all have their routines, habits, and cultures. With unexpected events, however, these old ways of dealing may fall short and new actions and knowledge may develop, at times somewhat reluctantly, due to resistance. As pragmatist philosopher William James wrote, "To a certain degree, therefore, everything here is plastic,"[17] meaning that even historically established ideas and practices need to prove their utility and relevance for the situation at hand. Then, even with unexpected events, a narrowing of experiences and actions may occur. What was an emergency becomes a recurring situation, and solutions and resources carry over from one instance to another. Some actions and experiences may develop into habits that suggest more appropriate responses. And at some point, there may become a standard way of managing the unexpected—perhaps a point where people have trouble imagining that there were ever other ways of reacting. Such routinization may occur even if people do not desire the reproduction of particular modes of dealing with problems. From a pragmatist perspective, then, at the most elementary level, a positive newborn screen is a prompt for collective action that runs against or along with established ways of dealing with issues. Newborn screening results become meaningful through the consequences they have for people, and it is through studying the consequences that we have access to the meanings, beliefs, and truths of newborn screening.

Acting under Uncertainty

The organizing mechanism of newborn screening is knowledge: knowing that a child has a metabolic disorder prior to symptom development should translate into preventive action. If diagnosis takes too long, it may be too late. Thus, newborn screening is expected to provide accurate