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Ask Me Later: Deciding to have clinical exome trio sequencing for my critically ill child

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Four years ago, my husband Scott and I sat in the pediatric intensive care unit (PICU) one evening with our 7-month old daughter Abby fighting for her life. A geneticist came in to have us sign consent forms for trio exome sequencing.

The hematology/oncology team, one of many care teams doing everything to save Abby, had recommended sequencing. They clearly explained that the results would not change her treatment or prognosis but might give us a clue as to why she was so sick. A reason was something that had eluded us for weeks, something I thought would help us make sense of this unfathomable situation.

What we knew: One day, Abby awoke listless and lethargic, no fever. These minor symptoms persisted for two days before she seemed to rebound. The next morning it was clear she had not recovered. Four days after a routine all-clear pediatrician's visit, we rushed to the hospital 45 minutes away. By the time of admission, everything had changed. Her skin was mottled and her fever had spiked to well over 100 degrees. Suddenly her bright blue eyes developed nystagmus as they turned dark and lost focus. Diagnosed with sepsis, she fought to live for two days before we transferred her to the hospital in Texas where she was born. As we prepared for the transfer, the doctor told us she had a blood clot in her brain. Her prognosis was uncertain when she arrived in Texas. She was unstable, with ongoing subclinical seizures and every system in her small body impacted by some infection. The source of the infection remains unclear to this day. Within a month, we learned that the clot was life-ending.

That evening in the PICU, the geneticist, sequencing consent documents in hand, asked about our familiarity with sequencing. I mentioned my work with Dr. Amy McGuire in the Center for Medical Ethics and Health Policy at Baylor College of Medicine conducting research in the area of ethical, legal and social implications of genetics and genomics. Over the last decade, I had been studying how other people make these kinds of decisions and react to learning this type of information. Now here I was facing the very same thing. The geneticist figured we did not need to hear much more, but I suggested he could continue. He paused, and when Scott did not ask any questions, he gave us the paperwork and left.

Competing Interests

The author declares no competing interests.

Ethics Declaration

M. Scott Robinson gave written consent to publish this paper.

My eyes glazed over looking at the consent forms filled with familiar, complex genetic jargon.¹ Embedded in the forms were several checkboxes to indicate, on behalf of Abby as well as our own forms for me and for Scott, our decisions about things like sharing our genetic data in public databases,² receiving variants related to recessive conditions that may be related or unrelated to the current medical issue, as well as receiving results not related to the current issue but for which there is established evidence of a causal relationship to other medical conditions.³

None of that mattered. Making those decisions for Abby was a no-brainer – we needed to do anything recommended to know that we had done everything possible. We had a “sign no matter what” mentality⁴ and did not hesitate to say yes to sequencing. We wanted any information that could help her or explain her condition. But, making those decisions for ourselves, especially to learn our own genetic information that was unrelated to the current issue, felt less urgent - an unnecessary burden of complicated decision-making during an intensely stressful time.

Before all of this, we turned down many opportunities to have genetic testing beyond the carrier screening and non-invasive prenatal testing we had done due to infertility issues and my age. While I was pregnant with Abby, a genetic counselor met with us to go over our unremarkable family history.

We learned that the cervical teratoma threatening Abby’s life and complicating delivery was caused by a germ cell mutation that happened for unknown reasons and was not hereditary. At the time, all agreed that it was okay that I did not want to learn what felt like unnecessary information through any additional testing.

We sat quietly amid the constantly beeping PICU machines. Scott turned to me asking, “What’s this list of 59 genes I could receive information about?”³ As well as I could, I explained that the list includes genes where there is enough evidence to have confidence that the gene is connected to a condition that you can do something about, if you know you have one that puts you at elevated risk. I added that it is complicated risk information because you can have a risky variant in the gene but not develop the condition, and vice versa. Then I said, “I’m going to check that box,” but would not check the box for carrier status because of our prior screening, and because I did not want to have more children. Scott signed his form without a word.

The next day while handing over our consent forms, I noticed Scott did not check a single box on his form. Scrawled across the top of his form in capital letters was “ASK ME LATER.” By the empty boxes, he wrote: “ASK ME LATER. I cannot make these decisions under emotional duress.” Nobody ever asked him later. No doubt the lack of checked boxes was simply interpreted as a “No” to return of results, as mentioned in the consent document written policy.

In the end, we were able to learn some of the information regardless of our choices. Because we had trio sequencing, Abby’s results report listed whether a gene variant found in her came from Scott or me. Nothing significant was found, but my curiosity was piqued when reading about the variants of uncertain significance that she shared with one of us. I also

wondered if he was at higher risk for something concerning that we could do something about had he opted to receive that information. When we could handle that information, would it be possible to find it out?

I know that ongoing studies on parents' perspectives of sequencing for their child generally report positive reactions, benefits seen as outweighing risks, and that parents are likely to feel a responsibility to agree to testing to do and learn everything possible.^{8,9} That all reflects my own experience quite well. But, it also misses some important points where it could have gone better.

How can consent documents be improved, especially given the complexity of the information and the many decisions that may be embedded in one document? Generally, I found consent documents to be a primary source to help me remember the myriad things signed off on during the stressful time. With a decade of studying the issues, I was able to understand the forms but wondered about people without that exposure or the specialized degrees required to understand the technical details. As sequencing is increasingly used, and more health care providers without specialized genetics training may discuss the information with families considering testing, simplified materials are critically needed to give patients and their families access to enough understandable information for an informed choice to be possible.^{1,4-7}

More work could be done to understand how parents are impacted by making decisions that are not for their critically ill child or relevant to the current condition. Future research could explore whether different approaches to consent form options and resources for future follow-up opportunities to learn non-critical information are needed for families of pediatric patients in critical care settings.

I particularly question whether all of the choices offered on these consent forms need to be made right then. While it seemed easy to decide to share my and Abby's information, deciding to learn about my own risk for something unexpected like a cardiac condition was less straightforward to me and impossible for Scott. While default approaches are low-cost and practical, including interpreting Scott's lack of checked boxes to mean "No," how do these approaches impact families and the family-clinician relationship? What about flexible approaches, like dynamic consent platforms that can be used to allow individuals to change their preferences over time for options like which of your results you want to know?¹⁰ These approaches present challenges as they are resource intensive for providers to set up and manage, and patients and parents must have access to and familiarity with computers and accessing medical records online. But, they might be one option to study whether they help patients/families defer non-critical decisions to a time when they are less overwhelmed.

When our results came back, three weeks later during Abby's last week of life, the geneticist mentioned I could come back within the next three years to learn my carrier status, despite my decision to not check that box on the form. I reflected on the practice of asking parents about their preferences for returning results up front.

Having seen Scott's words scrawled on the consent form, I couldn't help but wonder – why not ask later?

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