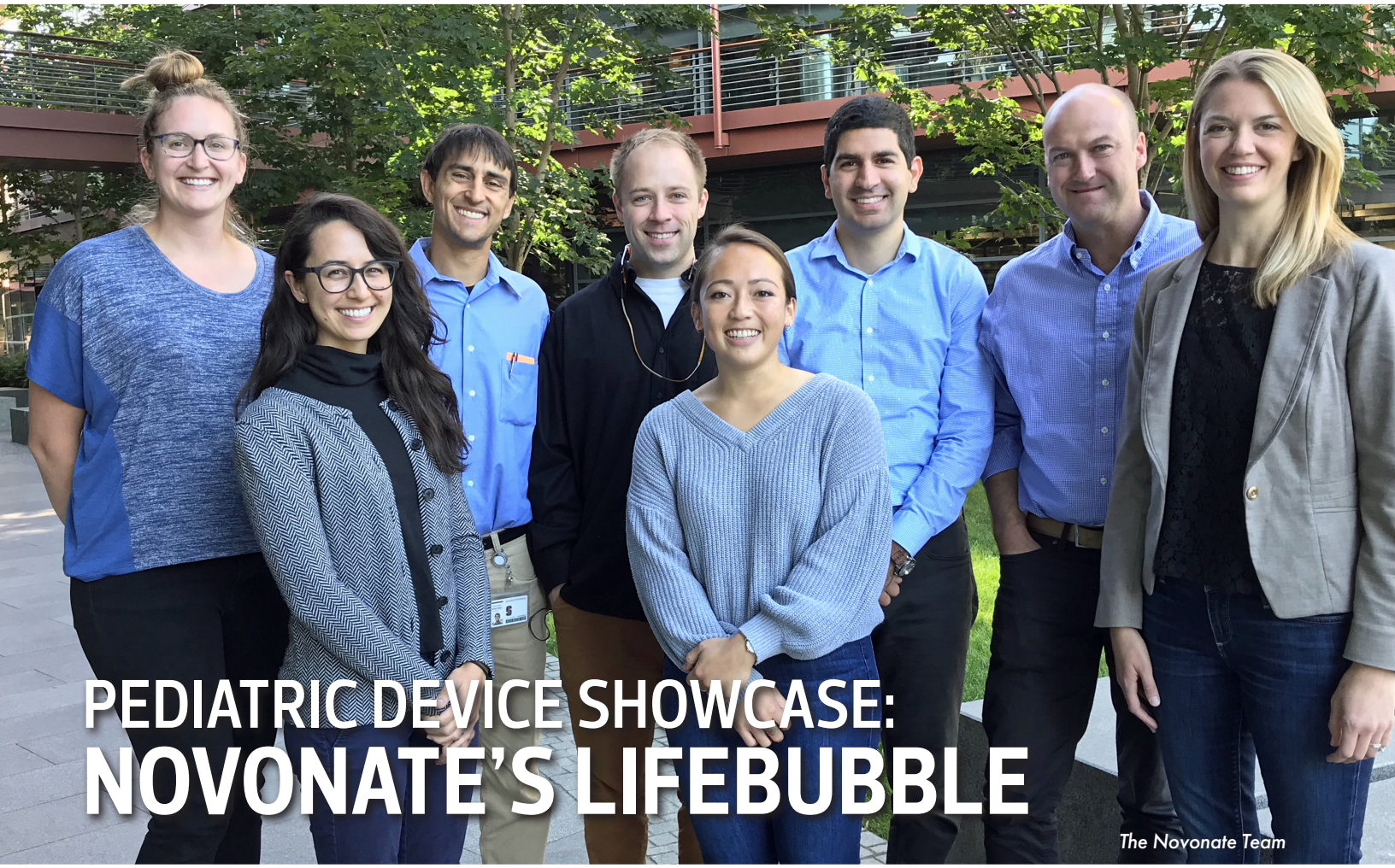

PEDIATRIC DEVICE SHOWCASE: NOVONATE'S LIFEBUBBLE

The Novonate Team

Novonate is a commercial-stage company dedicated to designing products that solve problems in neonatal care. The company is currently commercializing its first product, the *LifeBubble*, a novel device for the securement of umbilical cord catheters. Health Advances interviewed the co-founder and CEO of Novonate, Eric Chehab, PhD, to discuss the company's progress to date and advice for pediatric device entrepreneurs.

▶ ANDREW MILLAR, SHOUMYO MAJUMDAR, PHD, AND SUSAN POSNER, HEALTH ADVANCES

When healthcare providers hear "central line-associated bloodstream infection," they may instinctively think "never event." Never events are errors in medical care that are clearly preventable yet so serious in their consequences for patients that they should never happen. In 2008, Medicare included central line-associated bloodstream infection (CLABSI) in its initial list of diagnoses for non-payment, leading many providers to regard the complication as a never event. Since then, much has been done to prevent CLABSIs, including the institution of preventative care bundles and improvements in catheter technology. A significant amount of this progress, however, has focused on adult patients who may receive central lines for hemodynamic monitoring or long-term IV therapy, among other reasons. But when considering the impact of CLABSIs today, we may not immediately give thought to the hospital's littlest

patients—the neonates for whom vascular access is a critical part of their care.

Like many aspects of clinical care, vascular access, and specifically central line placement, is a completely different endeavor in neonates versus adults. To begin, neonates have a distinct access option that adults lack. That is, a freshly cut umbilical cord that has many unique advantages as a means of vascular access. Within the cord are two arteries and one vein, so when cut, it is essentially an open vessel to anywhere in the body. Moreover, there are no nerves in the umbilical cord, so access is completely painless for the baby. For these reasons, umbilical venous catheters (UVCs) are a reliable method of achieving vascular access in neonates up to the first seven days.

Despite their advantages, UVCs have been historically associated with high rates of complications, in part due to methods of securement that rely on sutures and tape. Notably, UVCs have a tendency to migrate and become malpositioned. While the incidence of malpositioning varies between hospitals, one study suggests that the rate could be as high as 68%. Case reports describe serious complications such as pericardial effusion, thrombosis, and hematoma in infants with migrated UVCs. Additionally, UVCs are associated with high rates of dangerous central line bloodstream infections, potentially due to umbilical cord catheters being the only central lines that are without a physical barrier around their insertion site. At the very least, malpositioned UVCs require additional imaging that increases radiation exposure.

The alternative to a UVC is a peripherally inserted central line or PICC, as some believe these to be less prone to complications. Evidence to support their use is not completely clear, though at least one guideline supports replacing an umbilical catheter with a PICC after seven days to reduce the risk of infection. However, PICCs come with their own problems for neonates and neonatal intensive care unit (NICU) staff. Neonates have notoriously small and difficult venous access, so they are more prone to insertion-related complications and are at higher risk for blockage with these devices than their adult counterparts—not to mention the pain inflicted with a PICC versus the painless umbilical route. UVCs therefore are widely recognized as an easier approach compared with peripheral access.

For the 200,000 or so babies who require central venous access each year, the result is a dilemma in vascular access. For quick and easy access, use a UVC, but face possible serious complications including infection. To potentially lower the rate of serious complications, use a peripheral line, but face a more challenging placement and risk complications at the time of insertion and pain for the baby.

Eric Chehab, PhD, founded a company in 2017 dedicated to solving this problem. The company is called **Novonate Inc.** and its first product, *LifeBubble*, is a silicone medical device used to secure and protect umbilical cord catheters to lower the risk of complications. Like other pediatric device innovators, Eric and the team at Novonate have had to navigate a challenging path to market, simultaneously tackling a unique unmet need and addressing a small patient population (in more ways than one). We spoke to Eric as part of an ongoing effort to showcase entrepreneurs innovating in the area of pediatrics.

ANDREW MILLAR

Andrew Millar (amillar@healthadvances.com) is an Engagement Manager at Health Advances, leading project teams for medical device companies and investors in Health Advances' Boston area office.

SHOUMYO MAJUMDAR, PhD

Shoumyo Majumdar, PhD, is a Senior Analyst with translational biomedical technology development experience in the Health Advances Boston Area office.

SUSAN POSNER

Susan Posner is a Partner at Health Advances and a leader of the MedTech practice. Susan has over 20 years of healthcare experience.

***Shoumyo Majumdar:* How did you decide to start Novonate?**

Eric Chehab: When I was a graduate student in a biomedical engineering course, my team was assigned a very broad topic of central line-associated bloodstream infections or CLABSIs—which are very dangerous and dramatic events. We started researching and got really interested in the pediatric space because we learned that the infection rates were a little bit higher, specifically with something called an umbilical cord catheter. We googled it and saw this catheter coming out of the belly button being held up by tape in midair. Our reaction was, "Wow, there's no way that's how it's actually done." We went to a neonatologist at Stanford and they said, "Yes, that's exactly how we do it." Later we found out umbilical catheters are one of the hospital's only unprotected central lines, so we decided we wanted to do something to solve this problem for neonates.

***Andrew Millar:* Why is it that umbilical catheters are the only unsecured central lines in the hospital?**

I wouldn't say they're necessarily the only unsecured lines. They are somewhat secured—with tape and sutures—but that securement is ineffective and becomes unreliable over time. But umbilical catheters are indeed one of the only unprotected ones; they are completely exposed. The first reason is because it is challenging to protect and secure a line that comes out at this unusual angle—roughly perpendicular to the skin. And the second is the umbilical cord needs to desiccate and dry off over time, so you cannot simply slap an adhesive over the top of it, because you would actually be promoting bacterial growth as it would be unable to dry out.

***SM:* So how does your product help solve that problem?**

We spent a lot of time interviewing nurses and neonatologists to understand their needs and design *LifeBubble*. The product allows the line to still come out at its natural angle and secures in a fully mechanical way by wrapping it around a securement knob and pulling an elastic strap over the top to lock it in place. It also physically protects the insertion site for the first time ever to prevent people's fingers from touching it while still allowing air flow through vents so the site can dry. Two hospitals have performed clinical studies with *LifeBubble* and found rates of malposition that were lower than previously reported in the literature, by a good amount.

***SM:* You mentioned developing a number of prototypes. What were the most challenging parts of the development process?**

We really try to stay in touch with our end user as much as possible. As engineers we had a good sense of the product requirements, but there were some designs we thought were really simple and they just didn't resonate with nurses. That was one of the hardest parts—digesting all the feedback and iterating, over and over again.

***AM:* Now that you have a product in place that is being used clinically, as you continue development, what do you expect to be your biggest challenges?**

At this point, *LifeBubble* has been used on over 600 babies, in five states, which is great. But we're now entering this early commercial phase of our company where we are trying to ramp up our commercialization capabilities. We don't have a dedicated salesforce yet. It has been me and our engineer, and now we have a nurse consultant leading the charge. But we need to strike some key partnerships and start accessing our market.

***Susan Posner:* What led to your success in reaching 600 babies and generating sales while still such a small company?**

We realized early on this was a pretty niche market in terms of size but a compelling clinical need that resonated with everyone we spoke with. One of my key advisors, James Wall, and I realized that we have to do this frugally. So we started applying for grant-based funding, pitching to micro-VCs and angel-type investors. We synched up with one VC and took some initial financing and then we were off to the races. We also received grant funding from the Pediatric Device Consortia and NSF. But the key is our awesome team. We had to have people who are Swiss army knives and excited to do things outside their expertise. That helps keep costs low while continuing to accomplish our goals, no matter what they are. And now as we hit the gas a bit, we're looking for some strategic partnerships as well, to see if there is a salesforce we can tap into.

***AM:* You mentioned one source of funding was the Pediatric Device Consortia. Congratulations on those awards. We would love to hear a little more about participating in that process and how you used that funding specifically.**

Our first PDC grant was used to get our initial R&D up and running. And we have received a few more that helped cover the cost of the molds and for manufacturing. The most recent award helped us establish a lot of our marketing efforts and support trials. I commend the FDA for recognizing the need to accelerate pediatric innovation and providing the grants to do it. While we have benefitted from the funding, one of the most rewarding aspects of the PDC has been connecting with other companies that are focused on the pediatric space.

***AM:* How has COVID-19 affected your ability to push Novonate forward? What have been the challenges?**

We did have to hit pause on fundraising for a bit as investors were trying to decide if they wanted to make new investments without the ability to meet people in person. We also lost access to NICUs almost overnight. But the silver lining is that it forced us to figure out how to support trials of our product remotely.

We've conducted completely remote training in several NICUs now, and to do that, we had to develop training materials and strategies that stand on their own better than before. So now we have a little more of a scalable training strategy, which I think is a really good thing.

SM: What's the future of Novonate as a whole?

Our overall goal is still more broadly to develop safe, innovative gold-standard products in neonatology. The next product that we're just starting to work on, and have received some funding for, is to secure endotracheal tubes in the NICU. It has a lot of the similar value propositions as *LifeBubble* and umbilical catheter securement, where endotracheal tubes for ventilated babies also move, leading to something called unplanned extubations. We are also working on improved adhesives. There is a need to adhere things to neonatal skin in a hot, humid environment like in an incubator setting but baby skin, especially if they are premature, is often unformed, so you cannot just use a more aggressive adhesive as you might in an adult.

AM: What would your advice be to other early-stage innovators in the pediatric space?

Stay in touch with the end users as much as possible and understand your stakeholder landscape as deeply as possible. Keep interviewing them and don't be scared of their feedback. It has helped a lot in this early commercial phase to be able to lean on the advice that we got from those bedside nurses early on. Now as we commercialize, we can point to specific features and say how they address user needs.

You have to understand all the different clinical stakeholders, too. In this space, bedside nurses are probably the most frequent end-users, but neonatal NPs are the ones actually placing the catheters and reading X-rays to detect migration. And the neonatologists are broadly responsible for the overall clinical issues in the unit. But the NICU nursing management is frequently the gatekeeper for our trials. Early on we thought the physician would be the primary stakeholder, eventually people said, 'you need to be talking to nurses.'

So, keep an open mind for sure, and of course always leverage the brainpower of founders of other companies. Sharing stories, bouncing ideas off of each other, and being a part of the community has been my saving grace in many ways. MTS

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