

GLOBAL HEALTH

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Pavkov speaking with a mother at a hospital in Bangladesh

Photo courtesy of Inspire

INSPIRE: Evaluating a Transition to Product Development

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THE PROBLEM/SOLUTION SPACE

Pneumonia is an acute respiratory infection that specifically affects the lungs.¹ Globally, pneumonia kills more children than any other illness.² In 2011, pneumonia caused 18 percent of all childhood mortality, or 1.2 million deaths in children under the age of five.³ Every year, it takes the lives of more children than AIDS, malaria, and tuberculosis combined.⁴ Despite its lethality and prevalence, pneumonia receives little attention relative to other diseases, and has been dubbed “The Forgotten Killer of Children” by the World Health Organization.⁵

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When a patient has pneumonia, the pulmonary alveoli that normally take in air during respiration fill with pus and fluid. The fluid interferes with the process of blood oxygenation and carbon dioxide exchange, making breathing painful and limiting oxygen absorption.⁶ When pneumonia is severe, the struggle to breathe can be life threatening, especially for young children.⁷ In developed countries, respiratory support is usually provided via mechanical ventilators. In resource-constrained settings, however, ventilators are often not available because of their prohibitively high cost.

Another approach, which has been used successfully for decades although it is not currently considered standard of care, is bubble continuous positive airway pressure (CPAP). Bubble CPAP delivers a continuous flow of humidified air with a high oxygen concentration via a pressurized breathing circuit and nasal prongs.⁸ Because bubble CPAP systems cost as little as 15 percent of the cost of mechanical ventilators,⁹ they are often used in resource-limited environments to provide respiratory support to children with severe cases of pneumonia. While bubble CPAP is an effective, low-cost alternative

to mechanical ventilators, its use still presents a challenge. Most bubble CPAP systems require oxygen tanks, which are expensive to transport to rural regions. The availability of oxygen is also unpredictable because of unreliable suppliers and poor road conditions. When oxygen tanks are unavailable, doctors cannot provide adequate care to children in acute respiratory distress.



Photo courtesy of Inspire

The Inspire bubble CPAP device

ABOUT INSPIRE

In 2011, Stanford University students Pamela Pavkov, Andrew Chang, Carey Lee, and Karen Lum enrolled in the project-based course, Design for Extreme Affordability. The program pairs teams of students with organizations operating in developing countries, with the goal of designing low-cost solutions to problems affecting the world's poorest people. The four students chose a

partnership with icddr,b, an international health organization in Bangladesh, to address problems surrounding childhood pneumonia. The icddr,b research hospital, located in Bangladesh's capital city, Dhaka, treats many children suffering from the condition. As defined by UNICEF, South Asia has the highest incidence of childhood pneumonia worldwide.¹⁰ Bangladesh alone has an estimated 6 million cases annually, giving it the fifth-highest global prevalence of the disease.¹¹

Pavkov and her teammates visited hospitals in Bangladesh to investigate needs surrounding childhood pneumonia and the challenges with using bubble CPAP as a treatment. "We went and talked to doctors, patients, nurses, families of patients; everybody who had in any way interacted with bubble CPAP or childhood pneumonia," recalled Pavkov.¹² "But we didn't know exactly what we were looking for, so we came back with way too much information and too many ideas," she laughed. Ultimately, however, guided by information from Dr. Saraswati Kache, a pediatrician at the Lucille Packard Children's Hospital at Stanford, the team decided to narrow its project to focus on bubble CPAP's reliance on oxygen tanks.

“Our first thought about oxygen, given the class focus on affordability, was that it is expensive to transport to rural locations. And then Dr. Kache, who had experience with bubble CPAP in the field, told us that when oxygen was available, it was often misused. Instead of blending room air with oxygen, many doctors used the system to deliver 100 percent oxygen.” The team knew that pure oxygen in excessive doses could cause deleterious side effects in children, including retinopathy (blindness) and asthma. “Dr. Kache told us that she had seen cases where bubble CPAP would have actually been effective without the oxygen,” said Pavkov. “And that was our key insight. We realized that CPAP without oxygen would dramatically reduce costs while maintaining the critical therapeutic effect of keeping the lungs open. And it would actually be safer than pure oxygen therapy.” The team decided to design a machine that would create the pressurized air of bubble CPAP without the cost, burden, and safety concerns that came with the oxygen tank.

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Pavkov and her team recognized that designing an oxygen-optional bubble CPAP device was a high-stakes proposal. “In addition to the engineering challenges, we knew there would be concerns around performance, adoption, and the need to prove why it represented a better approach,” she said. “But we purposely chose to go way out on the risk spectrum because, as students, the opportunity cost was low and the idea had home run potential,” Pavkov continued.

“So why not swing for the fences with a truly disruptive idea?” The fact that team member Carey Lee was a mechanical engineer, with the experience and technical skills to help the team build a functional prototype, supported this decision.

The team members dove into the project, which they named Inspire. When they began to conceptualize the design for the device, their first goal was simply to create a constant flow of pressurized air and the second was to figure out how to measure that flow. Both would need to be accomplished using widely available, inexpensive technologies, as mandated by the course. “We started with a balloon with weights on it, trying to measure the flow of air as it deflated,” remembered Pavkov. Subsequent iterations developed with guidance from Mike Strasser, a professional engineer at a design firm called Think2Build, involved a repurposed aquarium pump, which had the same function of creating air flow. “Carey was able to integrate that into what became our first prototype—a pump that pressurized room air and delivered it at a rate we could measure and adjust,” Pavkov said. “It was a classic example of using existing, low-cost materials in a completely novel way to achieve the desired effect.”

In addition to delivering a measurable, adjustable flow of room air, the prototype could also be attached to an oxygen tank in order to create an oxygen/room air blend that could be customized based on the needs of the patient. “We knew that 100 percent oxygen was dangerous, and that zero percent might not be optimal for some patients. So we wanted something that offered an adjustable mixture,” Pavkov stated. The team’s prototype was capable of running off a car battery, and, when used without oxygen, cost less than 1 percent of the traditional bubble CPAP treatments. When used with oxygen blended in at 50 percent, Inspire still reduced treatment costs by nearly two-thirds.¹³

The device’s potential was lauded by advisors at Stanford and physicians at icddr,b. However, there was still a great deal to accomplish to turn the prototype into a high-

performance, clinically appropriate device. After the academic year ended, Inspire team members applied for and received funding to continue working on the project. “We spent most of that summer refining the design we had developed, with the intention of taking it to the field to solicit feedback from its potential users,” Pavkov recalled.

Near the end of the summer, the team visited India, Bangladesh, and Vietnam with its prototype. “In Bangladesh, we took it to three locations: the icddr,b research hospital in Dhaka, a semi-urban hospital called MatLab that was an icddr,b affiliate, and an independent rural hospital called Lamb,” she said. The response from caregivers in the three environments was mixed. “At icddr,b and the semi-urban hospital, the doctors and nurses were excited by the science of providing respiratory support with less oxygen and felt that our device could be useful,” she noted. At the rural facility, however, where resources were so limited that they washed and re-used plastic tubing and disposable gloves, the caregivers were less enthusiastic. “Despite the fact that the need for a low-cost ventilation assist device was even more profound in the rural hospital, the doctors and nurses there lacked understanding of how oxygen-independent bubble CPAP might work,” reported Pavkov. “Despite the fact that Inspire could meet an urgent need, in the absence of clinical validation of the concept, they were unconvinced.”

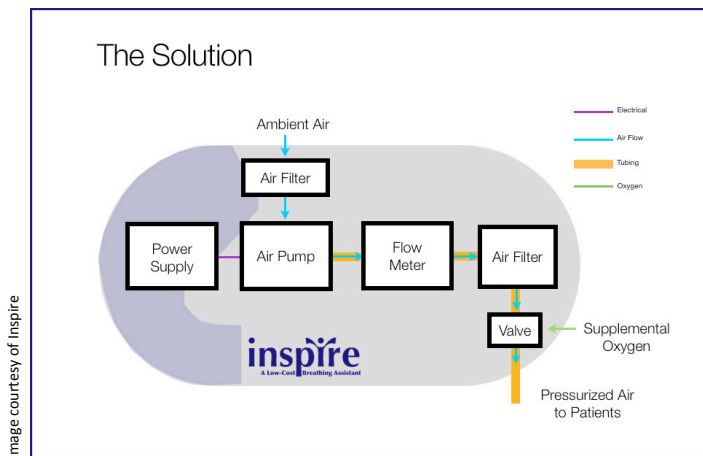


Image courtesy of Inspire

A schematic depicting the way the Inspire device works

These interactions in the field validated the potential demand for Inspire, as well as the need for clinical testing of the concept and an on-the-ground educational campaign to support its adoption. Importantly, the trip generated a “sea of feedback” that could help the team refine the design and further iterate the prototype. Pavkov and her colleagues returned to the U.S. to map out their next steps.

ONE CHALLENGE: EVALUATING A TRANSITION TO PRODUCT DEVELOPMENT

Despite the promise of the technology, the students realized that they were at decision point. Although the Design for Extreme Affordability course had spawned multiple companies, the team needed to carefully evaluate the commitment and risks involved in pressing forward. The challenges were significant, especially because medical device development was considerably more complicated and time consuming than many other forms of product development. “Compared to other products, medical devices have an exceptionally long-term horizon to commercialization,” said Pavkov. “The process takes 5 to 10 years—and that’s in the for-profit world. Developing a device for emerging markets or in a non-profit setting adds additional layers of complexity.”

The team anticipated that much of its time and energy would be consumed by the need for testing, regulatory approval, and clinical validation of an oxygen-optional bubble CPAP therapy. “With medical devices, the first thing you have to prove isn’t efficacy, but safety,” Pavkov noted. The team had returned from the field recognizing that they needed to do air quality tests to prove that ventilation assistance using room air would not cause harm to the patients. “This might actually be challenging in a place like Bang-

ladesh because the air is so humid and polluted,” she said. Subsequently, once the additional product development was complete, the team would have to bench test the device and all of its individual components, plan and conduct preclinical testing, and eventually, design and run clinical trials. “You can’t just put a device on a child and hope it works,” Pavkov emphasized.

Team members also felt strongly that if they were going to commit to bringing their product forward, they would have to move to a part of the world where bubble CPAP devices were being used in order to gain a deeper, first-hand understanding of the need and the users who could benefit from their solution. “Being in the field was a necessary precondition in my mind,” explained Pavkov. “If you’re not constantly talking to users and getting feedback, you’re not going to get the learnings you need to incorporate into your design iterations.” The team also recognized that they would need to be in the same geography in order to find local partners and build relationships with manufacturers, suppliers, and distributors. Additionally, they would have to devote significant time to understanding regional business practices, laws, and regulations. “Even when Westerners go in-country, they are still at a disadvantage in serving local markets,” Pavkov said. “Local partners are needed to provide cultural guidance and perspective, which is particu-

larly important when you’re talking to families about treatments for their children. There’s just so much we don’t understand.” The relocation requirements and the need for each team member to invest all of their time and efforts posed a challenge.



Photo courtesy of Inspire

The Inspire team: Pavkov, Chang, Lee, and Lum

THE SOLUTION: PUTTING THE PROJECT ON HOLD

After carefully considering the trade-offs involved in transitioning into development of a product designed for Bangladesh, the Inspire team determined that the majority of its members could not make the long-term commitment required to bring the project to fruition. “Andy was going into his fourth year of medical

school, and Carey and I had plans to start full-time jobs at the end of the summer,” stated Pavkov. “I wasn’t at a point in my life where I was prepared to move to India. And so we realized this was the end of the line.” Reluctantly, they decided to put the project on hold.

Reflecting on the experience, Pavkov said, “I think we would have benefited tremendously from an industry partner with medical device experience, so that we could have leveraged its design expertise and capabilities. Medical devices are a niche space in the design world with a lot of unique challenges. For example, unlike designing an irrigation pump, where you can do early user testing and rapid prototype iteration, in medical devices there is no ethical way to get that feedback until much later in the process.” She continued, “An industry partner with experience in testing, clinical validation, and commercialization could have helped us work through that.”

As of 2013, Pavkov and her teammates were still hoping to find the right team or company to take the concept forward. “Our hope at this point is to continue to get the word out to companies that develop medical devices, or people with an on-the-ground presence or expertise to take on a project like this,” she said. “We have all of our field research and the prototypes ready to hand off to the right person. We never had a goal to monetize the project—we’re just keen to see it get into the hands of somebody that can get it to the patient population that needs it.” ♦

NOTES

- 1 “Pneumonia: The Forgotten Killer of Children,” The United Nations Children’s Fund (UNICEF)/World Health Organization, 2006, http://whqlibdoc.who.int/publications/2006/9280640489_eng.pdf (March 19, 2013).
- 2 “Pneumonia Fact Sheet,” World Health Organization, November 2012, <http://www.who.int/mediacentre/factsheets/fs331/en/> (March 19, 2013).
- 3 Ibid.
- 4 Ibid.
- 5 “Pneumonia: The Forgotten Killer of Children,” op. cit.
- 6 Ibid.
- 7 Ibid.
- 8 Teresa Nowadzky, Alfonso Pantoja, John R. Britton, “Bubble Continuous Positive Airway Pressure, A Potentially Better Practice,” *Pediatrics*, 2009, 123; 1534, <http://pediatrics.aappublications.org/content/123/6/1534.full.html> (March 19, 2013).
- 9 “Continuous Positive Airway Pressure,” MANDATE: Maternal and Neonatal Directed Assessment of Technology, <http://mhntech.org/technology/technology-briefs/continuous-positive-airway-pressure/> (March 19, 2013).
- 10 “Pneumonia: The Forgotten Killer of Children,” op. cit.
- 11 Ibid.
- 12 All quotes from an interview conducted by the authors unless otherwise cited.
- 13 “Inspire: A Low-Cost Breathing Assistant,” openideo.com, http://www.openideo.com/open/how-might-we-improve-health-care-through-social-business-in-low-income-communities/inspiration/inspire-a-low-cost-breathing-assistant-for-infants-in-rural-settings-www.inspiremedical.org/gallery/inspire-pitch_final.pdf/ (March 5, 2013).