

# GLOBAL HEALTH

## Innovation Insight Series

*A doctor helps a pediatric asthma patient use the Respira Spacemask*



Photo courtesy of Respira Design

## RESPIRA DESIGN: Complex Requirements for a Simple Idea

STANFORD, CALIFORNIA

ESTABLISHED 2007

ERIC GREEN, SANTIAGO OCEJO,  
AND BARRY WOHL, CO-FOUNDERS

### THE PROBLEM/SOLUTION SPACE

Worldwide, an estimated 235 million people suffer from asthma,<sup>1</sup> a disease that causes chronic inflammation of the bronchial tubes (airways) of the lungs.<sup>2</sup> When an asthma attack occurs, bronchial swelling worsens and the muscles around the airway tighten, restricting the flow of air and causing frightening episodes of wheezing, chest tightness, shortness of breath, and coughing.<sup>3</sup> Although asthma affects people of all ages, the first symptoms usually develop before the age of five,<sup>4</sup> making it the most common chronic disease among children.<sup>5</sup> Asthma imposes a substantial burden on individuals and their families, and can severely restrict activities. Inadequate care over an extended period or delays in obtaining medical help during an attack can be fatal.<sup>6</sup>

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Although there is no cure for asthma, attacks can be controlled with inhaled medications that halt or prevent airway inflammation or bronchodilators that expand the bronchial tubes.<sup>7</sup> However, in low-resource environments, patients may have limited access to essential medications. For children in these settings, even when medications are available, effective delivery of the drugs to the lungs represents a significant challenge.<sup>8</sup> Asthma inhalers, which aerosolize the medicines, are difficult for young children to use because they require coordinating inhalation with a puff of medicine.

A device called a “spacer” can be attached to the inhaler to address this challenge by capturing the aerosolized medicine particles and holding them until the child’s next intake of breath.<sup>9</sup> While effective, spacers are often fragile and easily broken; and their small size makes them easy to lose, especially when carried by children. They are also relatively expensive, which means they are often unavailable in resource-constrained environments.<sup>10</sup>

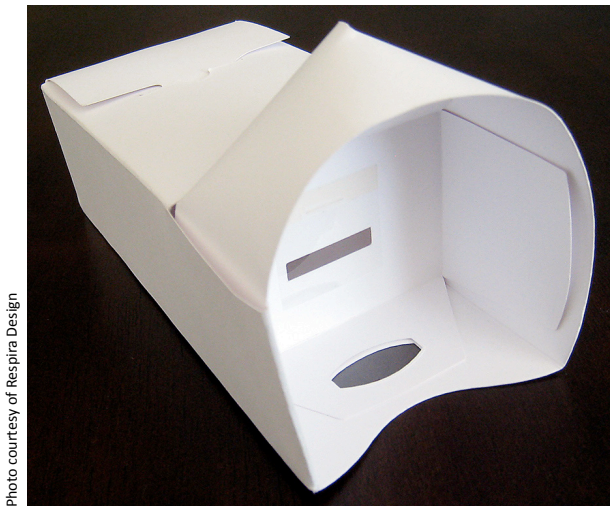


Photo courtesy of Respira Design

*The Spacemask device*

patient care in tertiary private and public hospitals, public primary care centers and clinics, and rural health facilities. They had a preliminary list of needs to start with, and planned to refine that list after completing their own in-depth observations. For two weeks, the students immersed themselves in these healthcare environments, watching procedures and talking to physicians, patients, and healthcare workers. By the time Green and Ocejo returned to Stanford, they had “more needs on the list than we started with,” recalled Green.<sup>11</sup> They conferred with their other team members and began to screen the needs they had uncovered. They prioritized them based on two key criteria: the magnitude of the potential health impact on the target population and the team’s likelihood of being able to develop a viable solution.

Through this process, one particular need rose to the top of their list. Green and Ocejo had observed that doctors in Mexico’s rural clinics sometimes had the medications they needed to treat their pediatric asthma patients, but lacked the equipment necessary to ensure that the aerosolized medicines reached the children’s lungs. “We saw a child come into one of the local clinics in the midst of an asthma attack,” explained Green. “And in order to get the medicine into the lungs, the physician put the medication into a

## ABOUT RESPIRA DESIGN

In 2007, Stanford University graduate students Eric Green and Santiago Ocejo took a course called Design for Extreme Affordability, which challenges students to develop affordable products and services for the world’s poorest citizens. Working in small teams, the students consult directly with course partners to identify needs and design solutions to real problems. In a first-time collaboration with Stanford’s Biodesign program, the 2007 offering of the course included projects focused on medical technology innovation. The students were partnered with Tecnológico de Monterrey School of Medicine (ITESM) in Mexico with the goal of addressing clinical needs in underserved communities in its surrounding areas.

To begin the needs finding process, Green, Ocejo, and a handful of other students went to Monterrey to observe

humidifier, which was not very effective. The need for this workaround and the desperation of the physician in this crisis was striking to us. We had been alerted that needs are often linked to workarounds and latent problems that cause stress and pain. I think that was very true for asthma,” he notes. The team decided to try addressing this problem.

However, before committing themselves to the project, the team members knew it was important to validate that their observations reflected a prevalent treatment issue that extended beyond the hospitals and clinics they had visited. “We reached out to our contacts in Mexico to explore treatment practices for childhood asthma and did some demographic research to learn how big of a problem asthma was there,” Green described. Focusing on patients without insurance, who were the most likely to utilize the rural health clinic network, the team learned that roughly 3.5 million uninsured children suffered from pediatric asthma in Mexico.<sup>12</sup> Moreover, because the workarounds available in the clinics often did

not get enough medication to the lungs to ease an attack, many families resorted to traveling long distances to the nearest emergency room, where spacers were more likely to be available. According to the team’s research, acute asthma attacks led to 1 million visits to Mexican emergency rooms annually, 90 percent of which could be managed by using an inhaler with a spacer.<sup>13</sup>

Convinced they were on the right track, the team continued its research by investigating the management of childhood asthma in the United States. They learned more about the specifications for spacers and how these

devices readily solved the problem of transporting medicine effectively into a child’s lungs. They also confirmed that existing products were unaffordable for resource-constrained facilities in Mexico and other developing countries. In combination, this information helped the team further refine its project approach. Rather than developing one device that would stay in the clinic and be used for multiple patients, they would try to create a low-cost version of a spacer that could be provided to each pediatric patient receiving inhaled asthma medication.

With this direction set, the team dove deeper into the treatment landscape by investigating the makeshift solutions being used in other low-resource environments. “Researchers at the University of Cape Town and the Red Cross Children’s hospital had studied the use of a low-cost spacer made from a plastic soda bottle,” recalled Green.<sup>14</sup> “And a study out of the University of Dundee in Scotland had measured the effectiveness of a cardboard tube in delivering medicine to the lung.”<sup>15</sup> Although these solutions met the course criteria in that they relied on materials that were cheap and ubiquitous in the places they wanted to serve, the Respira team was determined to do better. “We were focused on achieving best possible quality at the lowest possible cost. Our cost benchmark was the price of a plastic soda bottle,” Ocejo said.

As they began experimenting with different prototypes, they sought to minimize the cost of materials, as well as the cost of transporting the solution to providers and patients. “That led us to the idea of making something out of paper that would start flat and then could be assembled into a form, because that would be inexpensive to make and cheaper to distribute than a big, space-filling object,” said Green. “Initially we were rolling up the paper, but at a certain point we started folding it to create primitive, box-like models that looked a lot like the more expensive spacers that we use

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here in the U.S. And there was an ‘aha’ moment there. We started to think an idea like this could really work,” Green recalled.

Green and Ocejo shared their evolving ideas with physicians in Mexico, who were excited about the concept and worked with them to refine the preliminary design. As the course was concluding, the team had a rough prototype, a preliminary business plan, and growing certainty that they had “the seed of a potentially good solution,” Green stated. The other two members of their team were graduating and moving on but, for Green and Ocejo, the asthma spacer had become more than a class exercise. “Both the Biodesign program and the Extreme Affordability course had historically given birth to a number of projects that were successful in the real world, so it wasn’t unprecedented to be thinking about taking the idea forward,” Ocejo said.

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*The final version could be produced from a single sheet of paper. It could ship and store flat, and then be transformed into a usable spacer through a series of cuts and folds.*

#### ONE CHALLENGE: COMPLICATED TESTING FOR A SIMPLE IDEA

Green and Ocejo decided to explore the idea of further developing their device, which they had named the “Spacemask,” by entering it in the Ashoka Changemakers competition. This contest sought to identify disruptive innovations in health care. Simple, effective, and extremely low-cost, the Spacemask seemed ideally suited to meet the needs of pediatric asthma patients

and providers in low-resource environments, and the team was selected as one of three finalists worldwide. The competition generated some prize money as well as the attention of several nonprofit foundations, which expressed interest in the project. Even more importantly, the award gave Green and Ocejo the validation they needed to try moving their spacer from an unproven concept towards a market-ready solution. They formed Respira Design in 2009.

In terms of product development, the next step was to produce a working prototype with mechanical specifications for reproducibility. “At the time, I was making all of our prototypes by hand with an X-acto knife and a ruler,” laughed Green. To add much-needed engineering acumen to the team, Green and Ocejo reached out to Barry Wohl, an engineer and fellow student from the Design for Extreme Affordability course. “Barry not only had the engineering skills to make this into something of professional quality, but he understood everything we had done in Mexico and was connected to the project through the class,” said Green. Over the course of a year, Wohl developed 14 progressively more functional iterations of the Spacemask that were designed for manufacturing. The final version could be produced from a single sheet of paper. It could ship and store flat, and then be transformed into a usable spacer through a series of cuts and folds. It also included an innovative feature that created a better seal around the child’s nose and mouth to maximize efficiency, which the team believed would make its performance superior to existing low-cost solutions.

With the working Spacemask in hand, the team’s next challenge was to develop a testing strategy to validate its clinical utility. Green, Ocejo, and Wohl were committed to gathering data to understand the extent to which the device improved delivery of medication, and how many uses each device could sustain. They also had questions about durability to understand whether the spacer could still effectively deliver the aerosolized medica-

tion if it became crushed or bent. Finally, they were dedicated to studying whether the spacer would perform as intended in situations of emergency or distress. “This was a medical device that would potentially be used for someone who was having an asthma attack,” said Wohl. “We couldn’t put it in the hands of a mother to treat a child without a detailed understanding of how effective the device was in transferring aerosolized particles from the inhaler to the lungs. That was the minimum amount of clinical data we needed to be able to sleep at night.”

While the team could perform some preliminary testing on their own, they quickly discovered that the equipment they needed to conduct true efficacy studies would cost somewhere between \$10,000 and \$40,000, not including associated laboratory consulting fees. Hoping for a more cost-effective alternative, the team looked into hiring a contract research organization (CRO) with expertise in devices that worked with aerosols to do the tests. However, the service package the CRO offered would cost more than \$100,000.

From a regulatory perspective, the team did not need study results to make the device available in Mexico, but they felt strongly that quantitative data, especially on dose output, was critical in order distinguish the device from soda bottles, paper towel rolls, and the other improvised delivery methods being used in low-resource environments. Quantitative data could convince the customer of the reliability and repeatability of the device. “To me, the real shortcoming of the existing low-cost solutions was that it was a total shot in the dark as to how much medicine you were really getting out of them,” Green said. “So if we couldn’t quantify our delivery, we weren’t much of an improvement over the other workaround solutions.” To conduct these

tests, they would need substantially more funding. Unfortunately, they quickly discovered that would-be investors/donors wanted to see clinical data showing that the device worked as intended before making a sizable financial commitment. The team was in a quandary regarding how to proceed.

### THE SOLUTION: LEVERAGING CONNECTIONS AND TAKING A STEPWISE APPROACH TO TESTING

Feeling as though they were not yet prepared to pursue large-scale funding, the team entered its spacer in another business plan competition—the 2009 Stanford BASES Social E-challenge. Again, Respira was a co-winner of the event. The team used the funding that came with the award to manufacture the first run of 1,000 spacers that could be used to complete preliminary studies.

The prize money was not enough to proceed with a full complement of tests, so the team had to be selective. They started by leveraging Stanford connections to make contact with a local biopharmaceutical company, Nektar Therapeutics. At Nektar, they began working with an expert in aerosols, who also had deep experience in developing countries. At discounted rates, Respira was able to use Nektar’s equipment and existing as-



Photo courtesy of Respira Design

*A mother and child try the Respira device in a hospital setting*

says to design and execute an in-vitro testing protocol that provided enough feedback to help advance the design of the spacer in terms of making the mask fit better and improving aerosol handling.

Contacts at Nektar also connected the Respira team to the Catholic Healthcare West (CHW) Foundation for International Health. The foundation was planning an asthma study in a Guatemalan town that had an elevated occurrence of respiratory ailments. CHW was enthusiastic about using the Spacemask to help treat asthma exacerbations, and representatives collaborated with the team to design a pilot study of the device. The test would look at effectiveness, durability, and how users interacted with the Spacemask. None of the founders were able to make the trip, so they sent user surveys to Guatemala with CHW doctors and nurses. “We were particularly excited by the possibility of obtaining qualitative user data,” said Green. “We had the in vitro data telling us about the effectiveness of aerosol transmission, but that was really all the information we had. By letting CHW use the devices in Guatemala, we hoped to learn about user acceptance—whether people would be able to follow the directions and assemble it, and whether it would be perceived as a true medical device or some sort of substandard stand-in,” he stated.

While the Guatemalan study yielded some useful information, including verbal reports and photographs of people using the spacer, the Respira team ultimately got little hard data that would enable them to further refine or improve the Spacemask. “Things were a lot more chaotic than we anticipated and almost no surveys were returned. So we learned that it’s hard to get the clinical information you want if you are not physically present to collect it,” summarized Green.

In parallel with these efforts, the Respira team had tried pursuing funding from government entities, foundations, and impact investors in Mexico. However, they met with limited success due, in part, to investors’ desire for more information about the effectiveness of the device. Another obstacle was Respira’s business model. After considering whether to structure the company as a for-profit or nonprofit, the team had decided to pursue a for-profit social venture business model. “Our idea was to make the company self-sustaining to ensure that it could continue to deliver the products people needed,” explained Green. Unfortunately, while they identified Mexican investors experienced in philanthropic funding and found others well-versed in for-profit investments, the funding landscape for social enterprises was relatively undeveloped. “No one was comfortable with the idea of a social venture,” Green recalled.

Another concern was the team’s intellectual property (IP) status. With limited financial resources, the team had chosen to protect its IP only in the United States. “Our strategy was to get a patent in the U.S., where the IP regulations are the most stringent, with the belief that it would be respected elsewhere,” said Green. “However, it became clear that the investors were uncomfortable with the device being used in Mexico without explicit Mexican patent protection.” At this point, team members also faced competing priorities linked to their other career options. With no resources to further address these challenges, Green, Ocejo, and Wohl were ultimately forced to put product testing and the future of the Spacemask on hold.

Reflecting on the experience, Green highlighted the complexity of medical device innovation: “Even though our fold-up paper spacer was incredibly simple, rigorous testing was as essential for us as for any other medical device. Cost was on our radar from the

beginning, in terms of materials and distribution, but we didn't realize how expensive testing would be," he said. The team cautioned other medical device innovators to plan carefully for the time and expense associated with gathering user data in a safe and ethical manner.

Although the Respira team was not actively working on its device in 2013, Green, Ochoa, and Wohl continued to evaluate partnership opportunities and other possible approaches for bringing their low-cost spacer to underserved communities. For example, the team was considering an open-source model, making the device publicly available for others to use and improve upon. Although this would be a departure from the initial, for-profit business model, they felt that at this point, if they had a chance to make an impact on pediatric asthma, they should do so. "There is still a big need, and we still have a good design. We just have to figure out the best way to move it forward," Green concluded. ♦

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#### NOTES

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