In 2018, Sam Neff received the Exercise for Life Scholarship from the Boomer Esiason Foundation for his academic achievements, extracurricular activities, and having the fastest time among the finalists for a 1.5 mile run.

FEATURE STORY

By Jennifer Durgin

Taking on CYSTIC FIBROSIS

Seventeen years ago, Sam Neff began receiving care for his cystic fibrosis (CF) at Dartmouth-Hitchcock's Manchester, New Hampshire, clinic—90 miles south of the main medical center. At the time, his parents didn't know they were accessing a renowned team of physicians, nurses, scientists, and health-system researchers, all working toward a brighter future for families with CF. They just knew that they needed the best care for their son as close to home as possible. Today, Neff is a student at Dartmouth College, Class of 2021, and is making his own contributions to CF research.

To Sam Neff, "Living with cystic fibrosis is like running a marathon." He began running five years ago and is an avid cross-country skier. "You have to keep yourself healthy along the way," he says. In addition to regular exercise, Neff follows a daily treatment regimen. Every morning and every evening, Neff dons a black vest that shakes his torso to loosen the thick mucus in his lungs that's a hallmark of CF. He also takes daily antibiotics, probiotics, digestive enzymes, and a variety of inhaled medications to stay healthy and strong. Neff was diagnosed with CF when he was 6 months old and weighed a mere 11 pounds. Now, age 20, he's tall, athletic, and hopeful about his future and the future of the disease that's affected every day of his life.

"I think it's very important to project an image of strength, to have a positive attitude about the disease," explains Neff, who is shy by nature and only recently began talking openly about his disease. "If you project to others that you're healthy, then they don't feel that you're sick, and I think that rubs off on you."

Neff is the beneficiary of decades of collaboration by researchers, physicians, parents, and patients at Dartmouth's Geisel School of Medicine and Dartmouth-Hitchcock (D-H) and at other academic medical centers nationwide—all in partnership with the national Cystic Fibrosis Foundation. As a child, Neff stayed healthy through the persistence and dedication of his parents, Carol Ann and Ken, and the pediatric CF team at the Children's Hospital at Dartmouth-Hitchcock (CHaD). Now, as a student majoring in biochemistry (and history), Neff is analyzing genetic studies in one of the top CF research labs in the country, led by Bruce Stanton, PhD, director of the Lung Biology Center at Dartmouth's Geisel School of Medicine. Neff is also a patient in a clinical trial at D-H, which is testing a new triple combination of drugs to treat CF.

"Living with cystic fibrosis, it's very difficult to sit and wait for new scientific discoveries to happen," says Neff. "I wanted to make a contribution of my own."

FROM BIRTH

A genetic disease present at birth, CF affects the lungs and the digestive system and typically leads to a shorter lifespan. The primary problem is thick and sticky mucus that builds up in the lungs, clogging airways and promoting the growth of dangerous bacteria, fungi, and viruses. In the pancreas, the mucus prevents the release of digestive enzymes essential to nutrient absorption, leading to poor growth and difficulty gaining weight. As recently as the 1990s, most children with CF didn't make it to their 32nd birthday.

Thanks to advances in medications, treatments, and prevention, predicted life expectancy for individuals born today with CF is approaching 50 years. Cutting-edge science at Dartmouth and other institutions have made those advances possible; however, scientific discoveries and the medications that followed are only part of the story. The other major driver behind improving the health of children and adults with CF has been a nationwide quality improvement initiative that began at Dartmouth.

EVERY CHILD

In the late 1990s, Gerald O'Connor, PhD, DSc, then associate director of the medical school's Center for the Evaluative Clinical Sciences (now The Dartmouth Institute for Health Policy and Clinical Practice), began analyzing data from the Cystic Fibrosis Foundation's Patient Registry. O'Connor's analysis showed that a patient could live almost seven years longer depending on at which CF center they received treatment. While a center may have very good nutritional outcomes for their CF patients, that same center may have poor outcomes in measures of lung function, O'Connor found. Simply presenting the outcomes data to CF centers and showing them how their performance compared to other clinics spurred an unprecedented level of self evaluation and cooperation among physicians and nurses to improve care at their own centers and nationwide.

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The Cystic Fibrosis Foundation enlisted the help of O'Connor's colleagues, too: Paul Batalden, PhD, Marjorie Godfrey, PhD '95, and Eugene Nelson, DSc, MPH, experts in quality improvement and microsystems at The Dartmouth Institute. With the foundation's support, the team launched a multi-institution learning collaborative and quality improvement initiative, engaging clinicians, parents, and patients at more than 90 percent of the CF centers nationwide.

"Because of The Dartmouth Institute, we've had the opportunity to be at the forefront of quality improvement nationally," says Margaret Guill, MD, a pediatric pulmonologist and co-director of the New Hampshire Cystic Fibrosis Center at Dartmouth-Hitchcock.

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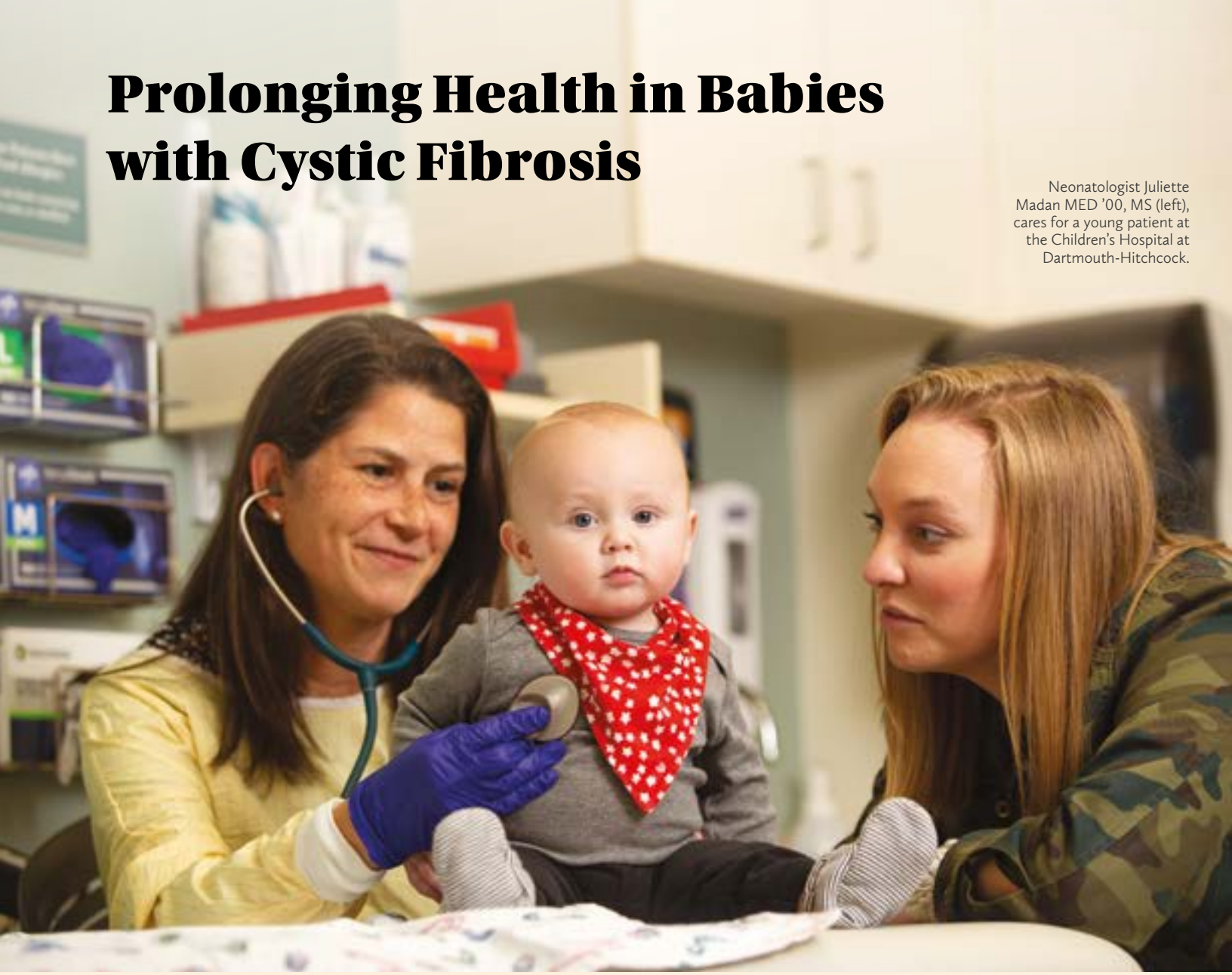
D-H pediatric pulmonologist and Geisel professor Margaret "Lou" Guill, MD, co-directs the New Hampshire Cystic Fibrosis Center with Brian O'Sullivan, MD. Sam Neff was a patient of Guill's for many years.

"Because of The Dartmouth Institute, we've had the opportunity to be at the forefront of cystic fibrosis quality improvement nationally."

Prolonging Health in Babies with Cystic Fibrosis



Neonatologist Juliette Madan MED '00, MS (left), cares for a young patient at the Children's Hospital at Dartmouth-Hitchcock.

"Newborn babies with CF are often indistinguishable from other newborns and are beautiful, healthy babies," explains Juliette Madan MED '00, MS, an associate professor of epidemiology and pediatrics at the Geisel School of Medicine and a neonatologist at Dartmouth-Hitchcock. The complications arise within the first weeks and months of life.

Abnormal populations of bacteria in the gut—known as dysbiosis—is a well-known complication of CF and contributes to impaired nutrient absorption. So Madan wondered, *What if we could tailor the microbiome of babies with CF to delay or prevent dysbiosis, train their immune system, and prolong health?*

To pursue that question, Madan and her scientific collaborator George O'Toole, PhD, professor of microbiology and immunology at Geisel, began studying the bacteria in the intestines and lungs of newborns and children with CF.

Madan started one of the first longitudinal CF infant cohorts in the country—a long-term study in which she has enrolled nearly every baby born with CF in New Hampshire since 2009. Her team collects intestinal and lung samples at regular intervals during the first years of life and then follows the children as they grow. The oldest participants are now 9 years old.

In collaboration with Geisel colleagues with expertise in bioinformatics and big data analysis, Madan and O'Toole have shown how bacteria in the intestines and lungs interact, and some of the mechanisms by which dysbiosis relates to the worsening of disease in individuals.

"The fact that a neonatologist can so easily and quickly partner with microbiologists and data scientists to pursue a brand new line of research is emblematic of the collaborative, nimble research culture of Dartmouth and its CF researchers and clinicians," says Madan.

The research team has also identified how the CF microbiome differs from the microbiome of healthy infants and young children, which could point to potential treatments. By identifying the missing microbes in CF that are important to training the immune system, Madan and her team hope to identify probiotic treatments to benefit infants with CF—giving babies with CF a better chance at a long, healthy life.

The Cystic Fibrosis Foundation's Quality Improvement Initiative continues today and is credited with increasing CF life expectancy by several years. The initiative has become a model for health care improvement in other diseases, too, by demonstrating the value of inviting patients and their families to partner with clinicians on the design and evaluation of care—and, most importantly, sharing data openly among centers, even when it reveals less-than-ideal outcomes.

Kathryn Sabadosa, MPH, a senior research director at The Dartmouth Institute and the mother of a young adult with CF, has helped lead the Quality Improvement Initiative since 2003.

"I wanted to ensure that every child with cystic fibrosis could get the best care anywhere in the country," says Sabadosa. Her son was cared for at D-H from day one. While every center has room for improvement, D-H has consistently provided high-quality CF care, as measured by the nutritional and pulmonary outcomes of its patients.

Today, Sabadosa is in awe of how self-sufficient her son Jack, now 18, has become at managing his CF. Like Sam Neff, Jack is athletic and healthy. He entered college this fall at Queens University in Ontario, Canada. The health of both young men is remarkable and the result of several factors: their own self-discipline and adherence to daily treatments and a healthy lifestyle, the dedication and support of their parents, and the excellence and seamless care of their clinical team at D-H, led by Guill and Brian O'Sullivan, MD.

"I knew Dr. Guill was looking at the whole person every time my son walked through the door," says Sabadosa. The relationships that she, her husband, and her son were able to build with the clinical teams has been crucial to his success, she says.

Sam Neff's mom, Carol Ann, who also has another son with CF, agrees.

"The fact that our boys are healthy and successful is truly a testament to the care they have received and continue to receive from everyone at CHaD," she says. "The doctors and nurses are always willing to answer every question we have, and we're so grateful for the relationships they have built with our sons over the years. Because of that, we know that the boys will be able to take fabulous care of themselves as adults."

MILES TO GO

While the health of young adults like Sam and Jack and the improved CF life expectancy are successes to celebrate, that's not the full win. Many children with CF still die before adulthood or live with damaged lungs. New CF medications—although remarkable in slowing the progression of the disease—target only some of the genetic mutations responsible for CF and don't clear the dangerous, persistent, underlying infections. And parents of children with CF still fear that their child will not live a full, healthy life. The marathon continues.

Just as they have for decades, researchers at Dartmouth's Geisel School of Medicine are among those leading the way to better treatments and a cure.

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Dartmouth College undergraduate Sam Neff (left) works alongside Bruce Stanton, PhD (middle), director of the Lung Biology Center at Geisel and the Andrew C. Vail Memorial Professor.

The Lung Biology Center's scientific success and impact lies in its multidisciplinary approach: microbiologists, biochemists, immunologists, neonatologists, pulmonologists, computational biologists, engineers, and data scientists working together to tackle CF from all angles—and from infancy through adulthood.

For example, pulmonologist Alix Ashare, MD, has teamed up with Jane Hill, PhD, a professor at Dartmouth's Thayer School of Engineering, to develop a breathalyzer for patients with CF. The device will identify which bacteria are growing in a patient's lungs by measuring metabolites in exhaled breath. That's essential and hard-to-obtain information that physicians can use to choose the best treatment for each patient.

In another collaboration, James Bliska, PhD, and George O'Toole, PhD, both professors of microbiology and immunology at Geisel, are exploring ways to engineer immune cells to better protect against harmful bacteria in the lungs of people with CF. Bliska also leads the Personalized Treatments for Cystic Fibrosis academic cluster at Dartmouth—a group of researchers including Stanton and three new endowed professorships funded through the generosity of donors.

"Our group is able to tackle cystic fibrosis from so many angles because we integrate so many different kinds of scientific investigators and clinicians," explains Lung Biology Center director Bruce Stanton, PhD. "We're big enough to have an impact but small enough to still be highly collaborative and nimble."

That ease of collaboration filters down to students, too.

"It was so easy to get involved," says Neff, who emailed Stanton halfway through his first year at Dartmouth to ask if he could work in one of the CF research labs. Stanton responded promptly and invited Neff to come meet with him. Although he had been a D-H CF patient since he was a toddler, Neff had no idea that he was joining a CF research community that had so intimately benefited his own life. Now, he plans to pursue a career in CF research and possibly attend medical school.

Just like training for a marathon, Neff is diligently building the scientific and academic skills he needs to pursue his dreams and contribute to the CF community at large. ■

WATCH A VIDEO ABOUT
Sam Neff and CF Research
dartgo.org/campaign-lung

A Hub for High-Impact Science

Geisel's Lung Biology Center is home to one of seven Cystic Fibrosis Research and Translation Centers funded by the National Institutes of Health. The center brings together over 200 scientists, physicians, and trainees to advance the understanding and treatment of CF and other chronic lung diseases. Their diverse expertise and interests yields an unusual breadth and depth of research projects.