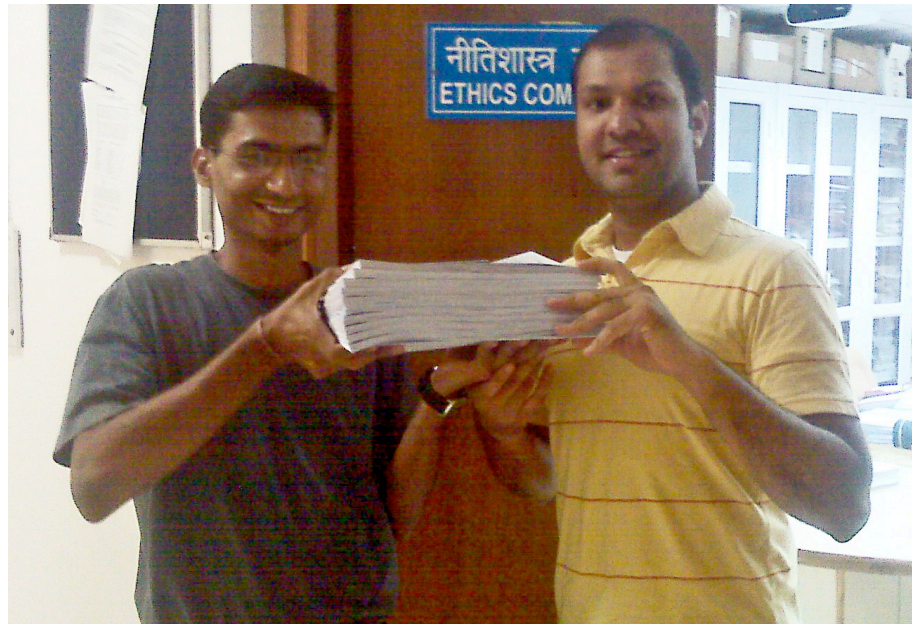


GLOBAL HEALTH

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Sharma and Chasmawala submitting their first-in-man clinical study protocols to the hospital ethics committee

Photo courtesy of Consure Medical

CONSURE MEDICAL II: Developing a Regulatory and Clinical Strategy to Support Global Growth

NEW DELHI, INDIA

INCORPORATED 2011

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THE PROBLEM/SOLUTION SPACE

Fecal incontinence (FI) is the inability to control bowel movements resulting in involuntary leakage or soiling.¹ The condition is believed to affect 8-15 percent of the general population, with the highest prevalence among the elderly^{2,3} and in acute and ICU care settings.⁴ FI is an intensely embarrassing and distressing condition, both for those who have it and for their caregivers. In high dependency settings, most solutions for FI are palliative and have significant drawbacks. Absorbent products such as diapers and pads

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are odorous and unpleasant, as well as time and labor intensive for caregivers in terms of product and bed linen changes. They are also associated with dramatic increase in the incidence of pressure sores⁵ and infections from skin breakdown due to contact with moisture or feces.⁶ One alternative, which can be used only in a medically supervised setting, is an indwelling catheter and collection bag.⁷ However, these rectal catheters are effective only when the stool is liquid or semi-liquid. They also are unpleasant for the nurses to manually insert and manage, can have issues with leakage, and may create complications from maintaining the rectum in an unnatural open position over an extended period of time.

ABOUT CONSURE MEDICAL

Experienced medical device executives Nish Chasmawala and Amit Sharma met while participating as fellows in the Stanford-India Biodesign (SIB) program, a partnership designed to facilitate medical technology innovation in India. During their time at Stanford, they became interested in FI as a compelling need with few good treatment options.

Upon their return to India, they further explored this need. After carefully evaluating the needs of the many stakeholders in FI care, they realized that the struggles of family members trying to care for loved ones with FI resonated with them the most personally. This scenario occurred frequently in resource-constrained environments like India, where elderly family members were often cared for at home rather than being placed in a long-term care facility. Accordingly, they founded Consure Medical and set out to develop a solution that would solve the problems inherent in existing FI treatments and be simple enough for a motivated family member to use.



Photo courtesy of Consure Medical

Sharma and Chasmawala prototyping in the lab in preparation for bench and clinical testing

With guidance from top doctors at the All India Institute of Medical Sciences (AIIMS), Consure Medical developed an indwelling device similar to a short-term implant. However, unlike existing rectal catheters which kept the rectum open at all times, the Consure solution diverted all fecal material from the rectum to an external collection device without interfering in peristaltic movements and other physiological functioning of the anorectal apparatus. It also had a slick insertion mechanism that allowed it to be placed in a clean and hygienic manner and was explicitly designed to be simple enough for a family member to use at home. Although developed specifically for the Indian market, the team quickly realized that the device had global healthcare applications and could deliver significant efficiencies within long-term and acute care settings. Not only was the Consure device more appealing to nurses than existing catheter-based solutions because of the ease of insertion, but it could reduce the costs of caring for FI patients because it could be placed without a doctor, imaging, or pre-insertion exam. Another source of efficiency was the reduction in time and labor associated with changing and cleaning patients who otherwise relied on absorbent solutions.

ONE CHALLENGE: DEVELOPING A REGULATORY AND CLINICAL STRATEGY TO SUPPORT GLOBAL GROWTH

Once Chasmawala and Sharma had developed a working product, their next challenge was to figure out a testing strategy that would validate the safety and efficacy of the device and support the company's regulatory strategy. With immediate opportunities to sell the product in India, as well as a larger global market to pursue, the team needed to think broadly about its clinical and regulatory approach. Consure wanted a plan that would give it license to operate in multiple geographies along with credible evidence to support adoption in multiple settings. "From our own product and market segmentation perspectives, we wanted to make sure that the product worked well, and to evaluate its use in different patient populations," said Chasmawala.⁸ "We knew we had a disruptive product that represented a new standard of care for the management of FI," he continued. "But we wanted the clinical data to prove it."

We planned to go beyond all clinical testing requirements in order to generate credible data that would support the global commercialization of our device.

An additional concern that Chasmawala and Sharma hoped to address through Consure's testing strategy was a general belief in the global marketplace that products from emerging countries were either "knock-offs" or inherently inferior. "Our product serves an unmet need in both emerging and developed markets by improving clinical outcomes and reducing costs," he said. "For Consure to realize its global potential, we had to overcome any perceptions of substandard quality."

THE SOLUTION: A MULTI-PART, PHASED APPROACH TO CLINICAL TRIALS

The strategy the team decided on involved gathering comprehensive and unimpeachable data on the safety and effectiveness of the product. "We planned to go beyond all clinical testing requirements in order to generate credible data that would support the global commercialization of our device," Chasmawala described.

To define a regulatory strategy, Chasmawala and Sharma relied on their industry experience, in-depth primary research, and the advice of a U.S.-based regulatory consultant. Based on the information they gathered, they determined that they should initially pursue clearance via the U.S. and European Union (EU) regulatory systems to give the company optimal flexibility in commercializing its product. As Chasmawala explained, the EU CE mark would enable Consure to sell the device in India after officially "notifying" the Drug Controller General of India. In addition, they would be able to use this clearance, along with the FDA's, to expand into the more lucrative European and U.S. markets, and also be well positioned to "go out and get regulatory approvals for all of the other key geographies that we intend to participate in," Chasmawala noted.

In Europe, the product was considered Class IIa. Within the U.S., Consure's product was classified as a Class II device, requiring 510(k) clearance. For both markets, Consure's strategy for clearance was based on the regulatory pathway established by multiple predicate devices. Accordingly, only limited data was needed to support the company's submissions, and obtaining data from human clinical trials was not mandatory. In fact, Consure believed it had already accumulated enough comprehensive benchtop safety data to satisfy the U.S. and EU regulatory requirements, and the team began working on its regulatory submissions.

Even though no clinical data was needed to potentially satisfy regulators, the team was committed to testing the device in real-world settings to further validate its safety and effectiveness and strengthen its credibility in the global marketplace. Although the company's ultimate goal was to have a product that could be used by patients and family caregivers in the home, Consure would start by testing its device in the medical environment where the team could more readily gain access to patients and more effectively include controls in its studies to ensure patient safety.

Early on, the Consure team had observed that because FI occurs in many different settings, numerous clinical specialties were involved in its treatment. According, they had assembled a multi-disciplinary team of advisors to guide them. "From the very onset of the project, we were working with cardiologists, a gastroenterologist, and intensivists [physician who directs care in the ICU] from neurology," Chasmawala described. "And because, as an indwelling device, the largest risk is internal bleeding or damage to other organs, we also had two leading GI surgeons on board as a precaution." The advisors not only helped Consure's team member understand how care was provided in the different clinical settings, but helped them develop an initial three-part clinical strategy.

According to Chasmawala, while the process of running clinical trials in India is fairly similar to trials in the U.S. and Europe, the medical device ecosystem is less developed. The Consure team had difficulty finding local clinical trial consultants with the appropriate expertise to help them. As a result, the team relied on their panel of doctors

to assist them in designing the trials. They wrote the protocols themselves, which they then verified with subject matter experts in the U.S. to ensure that they met U.S. and Institutional Review Board standards. "Our vision was to utilize a multi-part, phased approach with good safety nets in place to prevent any severe patient injury if there was an adverse event," he explained.

The three-part trial process would begin with a small first-in-man (FIM) study—a short-duration trial in which the device would be used on healthy patients scheduled to undergo routine colonoscopy. The primary goal of the FIM study was to prove safety in human subjects, although it also would generate some limited efficacy data. "The endpoints were focused on safety and validating the device from a conceptual standpoint," said Chasmawala. Specifically, they involved demonstrating that the doctors could place the device in the appropriate location in the body; that the product would work from a basic functional perspective; and that the doctors could retrieve the device from the patient without any harm or injury. "We were basically collecting data to demonstrate that everything we proved on the bench was actually happening inside the human body, too," he summarized.

The second trial would build on the data collected in the FIM study. "We would use that information to get to the next level of approval with the hospital ethics committee: 'We've done the safety study, now we would like to do a more complete efficacy study and show more explicitly how well our device works in target patients,'" he commented. While the Neuro ICU was chosen for the efficacy study in target patients, the team opted



Photo courtesy of Consure Medical

The Consure device

for non-acute patients in the ICU for risk-mitigation purposes. “In the ICU, non-acute patients have been in the unit for a few days. They are stable and passing stool,” Chasmawala said. “We didn’t want to start with patients that had multiple comorbidities and had just arrived in the intensive care unit.”

Once that data was gathered, Consure would use it as the basis for initiating a third trial. This last study in the plan would be the largest, involving a randomized selection of acute and chronic patients from both inside and outside the ICU. With few exclusionary criteria, the third test was designed to demonstrate that the device could be used on a broad patient population in different settings. It would also be designed to evaluate the effectiveness of the device longer-term.

With this plan mapped out, the Consure team sought approval to initiate the FIM study in the hospital where they had been working. Despite the small number of patients, short duration, and narrowly defined goals of this particular trial, Chasmawala encountered some resistance from the hospital’s ethics committee to undertake the study. “We have a ‘first-of-its-kind technology’ so the committee wanted to be cautious,” Chasmawala recalled. “They took some time to decide whether we were at an appropriate stage of product development to use the device in human subjects.” Ultimately, Consure was able to convince the ethics committee to approve the FIM trial based on “the caliber of our benchtop safety data,” said Chasmawala, as well as the strength of the trial protocols. “We had a good clinical plan in place to protect patients. Even if something went wrong, no one would be gravely hurt,” he added.

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As of February 2013, Consure had completed its FIM trial and successfully met its endpoints. The second test was underway, and approval for the third trial protocol was expected soon. The team had a commercialization plan for the established markets and a ‘seed the market’ strategy for its blue ocean markets. Once these studies were complete, Chasmawala planned to focus on health economic studies designed to prove Consure’s value proposition in different market segments and to support widespread marketing. “We’re designing a health economic study to learn more about our potential markets and to evaluate possible revenue streams. We will use that data to determine whether to consider taking on a strategic partner, or work with distributors to sell the product on our own,” he detailed.

While India would still be Consure’s first focus, the data from the study would help the team decide where and how to expand next. They hoped that by taking the product global, Consure would become a shining example of reverse innovation—a technology developed in an emerging market that also reduces cost and improves the quality of care in developed countries. Importantly, the team also remained committed to its original goal of serving the even larger population of geriatric patients residing at home. “Our second-generation product will be a little more consumer-centric for use in the home,” said Chasmawala. “We’re not there yet, but we will be.” ♦

NOTES

- 1 "Fecal Incontinence," National Digestive Diseases Information Clearinghouse (NDDIC), NIH Publication No. 13-4866, January 18, 2013, <http://digestive.niddk.nih.gov/ddiseases/pubs/fecal/incontinence/index.aspx> (January 28, 2013).
- 2 A.K. Macmillan, A.E. Merrie, R.J. Marshall, et al., "The Prevalence of Fecal Incontinence in Community-Dwelling Adults; A Systematic Review of the Literature," *Diseases of the Colon and Rectum*, August 2004; 47(8): 1341-9 <http://www.ncbi.nlm.nih.gov/pubmed/15484348?tool=bestpractice.bmj.com> (February 5, 2013).
- 3 William E. Whitehead, Lori Borrud, Patricia S. Goode, et al., "Fecal Incontinence in U.S. Adults: Epidemiology and Risk Factors," *Gastroenterology*, 2009; 137 (2): 512-517 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2748224/> (January 28, 2013).
- 4 D.Z. Bliss, S. Johnson, K. Savik, et al., "Fecal Incontinence in Hospitalized Patients Who Are Acutely Ill," *Nursing Research*, 2000 March-April; (49): 101-108, <http://www.ncbi.nlm.nih.gov/pubmed/10768587> (January 30, 2013); <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2614622/> (February 6, 2013).
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- 7 Ann Yates, "Managing Faecal Incontinence: A Joint Approach to Guideline Development," *Nursing Times*; 107: 12, 12-14, <http://www.nursingtimes.net/Journals/2013/01/18/v/f/m/290311Faecal-incontinence---a-joint-approach-to-guideline-development.pdf> (January 30, 2013).
- 8 All quotations from an interview with Nishith Chasmawala conducted by the authors, unless otherwise cited.