Blueshift RESEARCH REPORT

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Inspire Use Likely to Grow When COVID Subsides, Expansion Effort Pays Dividends

Companies: INSP, LIVN, NYXH

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Report Type: ☑ Initial Coverage ☐ Previously Covered ☑ Full Report ☐ Update Rating: 3.5/5

Research Question:

Can Inspire execute on its commercial expansion initiative to accelerate growth or is its implantable therapy a niche treatment?

Summary of Findings

- Inspire Medical Systems Inc.'s (INSP) minimally invasive hypoglossal nerve stimulation device for the treatment of moderate to severe obstructive sleep apnea (OSA) is not expected to experience significant growth until elective surgeries resume when the COVID-19 pandemic subsides.
- The Inspire system is a well-respected second-level treatment with very high patient satisfaction levels that is recommended for OSA patients that fail or refuse the standard of care solution, continuous positive airway pressure therapy (CPAP).
- Inspire's commercial expansion initiative—which includes direct-to-consumer promotions, physician training, surgery center expansion, and expanded insurance coverage—has had positive impact and use of the device is expected to grow. Patients and physicians are more aware of Inspire; however, it is still not considered a first line alternative to CPAP. One source commented that Inspire has moved its promotions online due to COVID-19 and they expect increased online promotions in 2021.
- Inspire's total available market (TAM) is considered accurate or even understated by most sources. CPAP failure is prevalent because of the lack of patient support and education after the CPAP device has been set up and delivered to the patient.
- Issues challenging increased use and adoption of Inspire include the lack of awareness of the treatment, despite the company's efforts; sleep center reluctance to inform patients of the option because of the potential loss of revenue; and the high upfront cost (a five-unit purchase totaling $125,000) for ear, nose, and throat (ENT) practices to offer the solution. One source said, if this is adjusted, the "sky is the limit" for the device.
- Two potential Inspire competitors—if they are successful in gaining FDA approval—are Nyxoah SA (NYXH), LivaNova P.L.C. (LIVN). Both companies are generating high interest levels because of their different approach to stimulating the hypoglossal nerve. One source referred to the Nyxoah device as a "smaller, simpler, better mouse trap."
- Pharmaceuticals are another yet-to-be-approved OSA treatment that hold promise and would be well received in the patient and treatment community. A clinical trial sponsored by Apnimed Inc. is currently under way in the United States.

Silo Summaries

1) Ear, Nose, and Throat Physicians and their Teams

Two Inspire users and one non-user think there are meaningful current and future growth opportunities for the company. Inspire's DTC promotions, including the use of patient and physician ambassadors, are raising awareness and will drive future growth. Inspire has produced excellent results and patient satisfaction is very high. **Inspire's estimated TAM could be understated, as one source said CPAP failure rates could be as high as 70%.** However, Inspire's cost for an ENT practice to become involved is prohibitive, requiring five devices at $25,000 each. If this is resolved, the "sky is the limit" for the device.

2) Sleep Center Professionals

Sleep center professionals were universal in their opinion that CPAP is the standard of care and first-line treatment for OSA. **There were varying opinions on a CPAP failure rate of 35%, which constitutes Inspire's TAM. Two sources said it is high, one said it is higher—closer to 60%, and another said 35% is accurate.** Sources were also mixed on the effectiveness of Inspire's commercial expansion effort, including DTC promotions. **One said it is raising patient awareness, another said it will generate growth if insurance coverage is strong, but a third said it will not work because surgery is a last resort for OSA.** This same source said with more research and patient/physician feedback, 80% of OSA patients will pick surgery.

3) Sleep Apnea Device Sales Channel

Inspire's published TAM is considered accurate or even understated, according to these four sales professionals working in the sleep apnea space. All four expect continued growth and increased adoption of Inspire's treatment by patients that fail or cannot tolerate CPAP. However, one source said until COVID-19 is less prevalent, Inspire's growth will not be significant. Two sources said Inspire's promotional efforts are effective and are raising awareness of alternative treatments for sleep apnea.

4) Industry Specialists

Two of three sleep industry specialists think Inspire's TAM is larger than the company has estimated and increased use of its implantable OSA therapy is likely. Inspire has generated strong clinical trial data from prestigious institutions, secured broad insurance coverage which requires a low copay, and its DTC outreach is driving high levels of patient interest and inquiries. **One source said he expects Inspire to generate strong growth for the next five years.**

	Inspire Expansion Initiative to Accelerate Growth	Patient Satisfaction with Inspire Treatment	Future Inspire Competition
Ear, Nose, and Throat Physicians and their Teams	↑	↑	Nyxoah
Sleep Center Professionals	→	↑	LivaNova & Pharmaceuticals
Sleep Apnea Device Sales Channel	↑	↑	Nyxoah & LivaNova
Industry Specialists	↑	↑	Nyxoah, LivaNova, & Pharmaceuticals

Background

Blueshift Research's initial research found Inspire working to accelerate the use and adoption of its Inspire system for the treatment of obstructive sleep apnea. Direct-to-consumer (DTC) advertising, increased physician outreach and sales efforts, the addition of new treatment centers, and increased reimbursement coverage are all being used to expand the commercialization of Inspire's unique implantable device. The system is used primarily by the 35% of patients who fail with CPAP. Successful execution of Inspire's expansion initiative will require significant patient and physician education to move the Inspire system beyond its niche market position, while also navigating the resistance to the high costs related to the device and associated surgery.

Inspire offers the only FDA-approved neurostimulation solution for moderate to severe obstructive sleep apnea. The Inspire system is a minimally invasive implantable device. It is a closed-loop solution that continuously monitors a patient's breathing and delivers mild hypoglossal nerve stimulation to maintain an open airway.

The Inspire system was approved by the FDA in 2014 and, since then, more than 10,500 patients have been treated with the device. Since Inspire's IPO in May 2018 the company has significantly increased reimbursement coverage from 2 million to 207 million covered lives and expanded its Medicare coverage to all 50 states. With this strong foundation of coverage, Inspire is expanding its commercial efforts to drive continued growth and utilization of its Inspire system.

According to Inspire, the TAM for its Inspire system is significant. Annually, approximately 17 million individuals in the United States are diagnosed with moderate to severe OSA. Two million of them are prescribed a CPAP device, of which 35% or more (700,000) fail or do not comply with the treatment. Inspire estimates that 500,000 of these patients are candidates for an Inspire system, which creates a market opportunity of $10 billion. (Average selling price for Inspire, including surgery, is $30,000 to $40,000.)

Inspire reported strong third-quarter (Q3) performance and made meaningful progress with its commercial expansion program. Revenue increased 72% year to year to $35.8 million, fueled in part by a backlog of implant procedures postponed due to COVID-19 surgery restrictions. Inspire opened 42 new treatment centers during the quarter, bringing the total to 370, and it plans to open 28 to 30 more in Q4. Seven new sales territories were added, with six to seven additional regions scheduled to be added in Q4. Two national contracts with ambulatory surgical centers were signed and additional insurance coverage was obtained from several commercial payers.

Blueshift spoke to two ENT practices around Philadelphia offering Inspire to their patients who fail on CPAP devices. Over 20 patients have received the Inspire system at one practice and all report high levels of satisfaction. The other is a new Inspire provider and its handful of patients are also performing well and happy with the therapy. A general practitioner in the same area said he has referred hundreds of patients for sleep apnea treatment over the years and only one has been prescribed the Inspire device. He said the patient responded positively to the treatment after they adjusted to the discomfort from the stimulation and are now highly satisfied. The source views the device as a niche treatment that will move into the mainstream as its science continues to improve and its prohibitive cost declines.

Current Research

Blueshift Research assessed whether Inspire can execute on its commercial expansion initiative to accelerate growth or whether its implantable therapy a niche treatment. We employed our pattern mining approach to establish five independent silos, comprising 15 primary sources and five secondary sources focused on sleep apnea treatment. Interviews were conducted November 23–December 4.

1) Ear, nose, and throat physicians and their teams (3)
2) Sleep center professionals (5)
3) Sleep apnea device sales channel (4)
4) Industry specialists (3)
5) Secondary sources (5)

Next Steps

Blueshift Research will continue to research the Inspire expansion initiative to determine if it is successfully gaining market share. We will also monitor potential competitors to see if they are gaining traction outside the United States, where they are approved for use, and the progress they are making in gaining FDA approval.

Silos

1) Ear, Nose, and Throat Physicians and their Teams

Two Inspire users and one non-user think there are meaningful current and future growth opportunities for the company. Inspire's direct-to-consumer promotions, including the use of patient and physician ambassadors, is raising awareness and will drive future growth. Inspire has produced excellent results and patient satisfaction is very high. However, the patient selection process, procedure, and post-surgery titration is a two- to three-month process and considered a treatment of last resort. Inspire's estimated TAM could be understated, according to the non-Inspire user, as he said CPAP failure rates could be as high as 70%, but Inspire's cost for an ENT practice to become involved is prohibitive, requiring a purchase of five devices at $25,000 each. If this issue is resolved, he said the "sky is the limit" for the device. Nyxoah was discussed by this source as a future competitor, along with future surgical procedures that he is involved in researching.

Key Silo Findings

Background

- 2 sources' practices offer Inspire device therapy.
- 1 source found Inspire's startup costs prohibitive.

Inspire's Commercial Expansion Initiative

- 3 said Inspire has significant growth potential.
  - 1 said Inspire's pre-COVID-19 DTC promotions, including TV, radio, and in-practice meetings using patient ambassadors, were raising awareness and they expect them to continue virtually in 2021.
  - 1 said Inspire's effort to certify more ENTs and surgeons to perform the procedure will increase usage.
  - 1 said, if Inspire can address the high practice startup cost, the sky is the limit for growth.

Inspire's Treatment

- 3 said the Inspire treatment was effective and had high patient satisfaction levels.
  - 1 said patients are so happy they want to put her in their will.
  - 1 said patient satisfaction is high and she would recommend it to anyone that has failed on CPAP.
  - 1 said Inspire is an effective treatment of OSA, but not a quick fix. It takes two to three months from procedure through recovery and titration. Inspire will get competition from Nyxoah and eventually other surgical procedures, which he is helping to research.

1) Head nurse at an ENT practice in the East with more than 120 Inspire implantations

Inspire has high patient satisfaction at this ENT practice. Patients comment they want to put this source in their will and would never go back to CPAP. Before COVID-19, they were active with regular events promoting the new Inspire therapy with Inspire patient advocates and "ambassadors" giving testimony of their change in quality of life. They continue to do virtual programs—Zoom meetings—and plan to do more in 2021. As this is new and unique for OSA patients, the source perceives Inspire as a high-growth product responsive to increased promotion and patient knowledge.

Background

- "Our practice was the first approved in the state to conduct the Inspire implants. It is the busiest Inspire center in the tri-state area of New York, Connecticut, New Jersey. We have performed 124 procedures since our ENT was approved."

Inspire's Commercial Expansion Initiative

- "The numbers Inspire states as the potential for patients is hard to gauge; like anything new, it takes time. This has only been available a short time."
- "This is a growth area. There have not been good alternatives to CPAP. This represents a new alternative that appeals to many dissatisfied OSA patients."
- "Now that it is on TV and getting radio spots, more people know about it and are talking about it. There are a growing number of educational forums to spread the word. We used to do these programs in the office, in person—prior to COVID. We would advertise, bring in prospective patients, and have Inspire implanted patients and the doctors talk to this audience about the procedure and the post-surgical change in their quality of life."
- "Inspire identifies advocates who have had the procedure, names them as 'ambassadors', and makes them available for meetings—in person and, this year, virtually, on Zoom meetings. They have been well received and spread the word."
- "Inspire was more active with events prior to the pandemic but is now planning to do more in 2021 using Zoom and similar ways to get to more potential patients."

> **Our patients are the most satisfied. I've had many of the Inspire patients tell me they are putting me in their will.**
>
> *Head nurse at an ENT practice in the East with more than 120 Inspire implantations*

Inspire's Treatment

- "Our patients are the most satisfied. I've had many of the Inspire patients tell me they are putting me in their will."
- "Not every patient is ecstatic after the surgery but, if you ask any of them if they would like to go back to CPAP, they all say, 'no way.'"

2) ENT office manager in the Southwest

This practice is experiencing excellent results with Inspire, with extremely high patient satisfaction. Patients are driving three to four hours to come to their practice, get assessed, and have the procedure. This procedure is still very new and most OSA patients have not heard about it. This source believes, as patients hear more about this alternative to CPAP and more ENTs get trained, it will have significant future growth.

Background

- "We have been doing the Inspire procedures for the past two to three years with excellent results."
- "We have completed about 30 Inspire implants. Many of the patients are coming from three to four hours away to have the procedure by our ENT."

Inspire's Commercial Expansion Initiative

- "[It is] hard to know about the accuracy of the Inspire patient potential numbers but this should really grow over the next few years. It's still a new procedure."
- "Most patients are approved by insurance—the majority. It is a process of elimination, as some patients just do not qualify and this is not the right procedure for them. There are many criteria that must be satisfied in order to be approved, dealing with the patient's AHI [apnea-hypopnea index], their tonsils, their uvula—anatomic and physiological criteria."

- "I think the use of [Inspire] will experience significant growth, especially as more ENTs and/or surgeons learn about it and get certified. There are very few practices in this area that are doing or can do this procedure. As there is more information to OSA patients available, there will be more patients asking their sleep doctors and other healthcare professionals about this therapy."

Inspire's Treatment

- "Patient satisfaction is extremely high. You get a few one-offs, especially right after surgery, but almost all resolve and patients are grateful for the results."
- "There is no competition at this time. If a patient fails on CPAP, the other alternatives are oral appliances and, perhaps, weight loss for OSA."
- "I would recommend Inspire to anyone who is failing or can't tolerate CPAP therapy. We may be in Oklahoma but, for any patient in need, it's worth the trip to see our doctor and have this procedure."

3) ENT surgeon on the West Coast

This ENT surgeon does not perform Inspire. The cost of program startup was prohibitive. The Inspire procedure is a good one, but not a quick fix. Implantation, titration, and recovery is a two- to three-month process. Inspire has competition coming shortly. Nyxoah is on the horizon and this source is actively involved in early research into another surgical intervention for OSA. The 35% CPAP failure estimate is low. This source estimates failure at 70% but believes that with proper patient education the success rate could be elevated to the 80% to 85% range. Inspire is considered a last resort, but the company's DTC efforts have been raising awareness. If the startup costs for the technology becomes more manageable for smaller facilities, the sky is the limit.

Background

- This ENT surgeon does not currently perform Inspire but does a lot of OSA surgeries and is part of an upcoming study evaluating a new surgical technology developed by a group of academic surgeons (currently unfunded).

Inspire's Commercial Expansion Initiative

- "When Inspire first started marketing to practitioners [including hospitals and surgery centers], they required a significant upfront investment. Cost of entry to the program was the purchase of five $25,000 devices [$125,000 total]. Many facilities were not in the position to make that kind of investment."
- "As much as I think Inspire is a good treatment, it was not a good fit for private practices and ambulatory surgical centers, due to the upfront investment. Although, I am not certain whether or not Inspire has changed that policy."
- "Inspire will not be the only game in town for very long. In addition to Nyxoah, I am involved with a group of academic surgeons for a surgical technology in the basic research phase presently."
- "Thirty-five percent CPAP failure is an underestimation. In my experience it is more like 70%. There are a lot of reasons people fail with CPAP, including lack of education, user unfriendliness, claustrophobia, need to travel, etc."
- "Based on my own market research, the biggest deterrent for CPAP alternatives is simply that people are unaware that they have other options. I think more people would be open to alternatives, even surgery, if they better understood what is available. In this respect, I think Inspire's DTC efforts will be effective."
- "OSA is a very heterogenous condition. It is complicated and multi-factorial anatomically and physiologically. I am skeptical whether a pharmaceutical would be effective. But, to be clear, CPAP is a band-aid. It does not fix the problem."
- "If patients were to be better educated and trained, I believe the CPAP acceptance rate could be in the 80% to 85% range. But sleep centers and DMEs [durable medical equipment companies] do not get paid to educate. So they don't. That said, Kaiser Permanente has had a pretty comprehensive CPAP patient education service. Although they hoped it would dramatically improve compliance, there is still a high dropout rate. For some, CPAP is a lifesaver and they are motivated to make it work; for others, it is simply too much of a burden without adequate perceived benefit."

> **Inspire has been successful in getting the word out and softening the market for a surgical intervention. If the company can better adjust to working in the ambulatory setting [with a reduced startup cost], the sky is the limit.**
>
> *ENT surgeon on the West Coast*

- "Inspire has been successful in getting the word out and softening the market for a surgical intervention. If the company can better adjust to working in the ambulatory setting [with a reduced startup cost], the sky is the limit."

Inspire's Treatment

- "There are a lot of steps between OSA diagnosis, first-line therapy [CPAP], and Inspire, which include dental appliances. Once a patient progresses to Inspire surgery it can take up to eight weeks to properly titrate and then another sleep study is performed. The whole process, including recovery, is a two- to three-month time investment. It is not an overnight fix."
- "Inspire is a significant procedure—more of a last resort—and it is not without its own maintenance. Although the battery life may have improved in the last few years, the recommendation initially was to replace in five to six years."

2) Sleep Center Professionals

Sleep center professionals were universal in their opinion that CPAP is the standard of care and first-line treatment for OSA. The CPAP failure rate of 35%, which constitutes the Inspire TAM, generated a variety of opinions. Two sources said the failure rate is too high, one said it is actually higher—closer to 60%, and another said 35% is accurate. Sources were also mixed on whether Inspire's commercial expansion effort, including DTC promotions, is effective. According to one source, it is raising patient awareness, another said it will generate growth if insurance coverage is strong, but a third said it will not work because surgery is a last resort treatment for OSA. This same source said, in time, with more research and patient and physician feedback, 80% of OSA patients will opt for surgery. Two sources acknowledged that patients that receive the Inspire device are highly satisfied with the results. One source said sleep physicians and sleep centers have a conflict regarding referring failed patients for surgery as it could negatively impact their revenue. Future competitors that Inspire will have to face include LivaNova and pharmaceuticals.

Key Silo Findings

Background

- 1 sleep center offers CPAP, oral devices, and surgical options including Inspire.
- 1 university-based sleep center is an approved Inspire treatment center.
- 1 sleep center specializes in oral appliances.
- 1 sleep center outside the United States said Inspire is not a first-choice treatment for patients that fail CPAP.
- 1 sleep center only treats patients with CPAP.

Inspire's Commercial Expansion Initiative

- 1 said DTC promotions are not effective, as physicians make the treatment decision and surgery is the last option.
- 2 said Inspire's DTC is raising awareness. 1 added that if insurance coverage is strong it will increase usage.
- 1 said Inspire's broad insurance coverage is a positive and young patients will be more likely to opt for surgery.
- 1 did not comment.

Inspire's Treatment

- 1 said more research, patient and physician feedback, and time is needed for Inspire's treatment to gain share. They added that, eventually, 80% of OSA patient will opt for surgery.
- 2 said Inspire patients are highly satisfied with the treatment.
- LivaNova and pharmaceuticals are expected to be future Inspire competitors.

1) Manager of a West Coast diagnostic sleep center

Although Inspire offers a respectable alternative to CPAP machines, it will take years before the medical community and insurance companies promote surgical procedures for sleep apnea. According to this source, CPAP is the king of OSA treatment and the go-to solution for most practitioners and patients. The increased DTC advertising campaigns are not effective since treatment decisions are driven by medical providers and insurance companies. More research, more feedback, and more time are required before doctors will confidently prescribe surgical procedures. Over the past nine months, this clinic performed two surgical treatments compared to 225 CPAP referrals, so it is unlikely Inspire can significantly increase market share in the short term.

Background

- "We offer CPAP, oral devices, and then surgical options as a last resort."
- "We use Inspire Medical Systems and are looking into LivaNova."
- "In the last nine months we performed two Inspire surgeries vs. 225 CPAPs."
- "Compliance is the biggest problem with CPAP because they have to carry it around."
- "CPAP is usually the first option; oral devices are second, and the least successful treatment. Oral devices do not work well and they are uncomfortable. Surgery is usually the last option."

Inspire's Commercial Expansion Initiative

- "Their TAM claim of 500,000 potential patients annually seems a bit high."
- "Inspire's direct-to-consumer marketing is irrelevant if doctors are not pushing or supporting it. Since Inspire's treatment must be prescribed by a physician, the patient has little choice in the matter, so they should focus their marketing campaigns on providers."
- "New technologies take a while to catch on. It took Tesla years before the electric car became a thing."
- "Although LivaNova is a competitor, CPAP is the king in OSA treatment."
- "[Inspire's] primary roadblocks to growth are the perceived risk-reward factors by doctors and patients."

Inspire's Treatment

- "I haven't heard any patient complaints so far, but it's too soon to tell."
- "In time, 80% of OSA patients will opt in for surgery."
- "Inspire cannot do much to overcome surgical reluctance. It is a waiting game and only time will tell."

2) Physician with a West Coast university-based sleep medicine department

This sleep medicine-specialized physician is confident that true CPAP intolerance is much lower than 35%. He describes a broken medical system as the primary source of failures, where most patients do not receive the training they need to succeed with CPAP. With the increased availability of specialized sleep centers and coordinated medical care, he expects CPAP successes to increase over time. More patients are presenting to the center with knowledge of Inspire, suggesting that the direct-to-consumer efforts are raising awareness. However, this source strongly encourages CPAP as a first option for which educated patients enjoy good success. LivaNova is an investigational technology not currently available in the United States and Respicardia Inc.'s remedē System treats central sleep apnea (CSA), rather than OSA. The more promising option could lie in pharmaceuticals.

Background

- "My academic facility is an Inspire Center. I have been here for nearly two years but the Inspire technology preceded me."
- "When I recommend Inspire it is usually the result of CPAP intolerance and failure with both dental appliances and positional therapy. Although there are some patients diagnosed with OSA who, as soon as the discussion of CPAP comes up, they refuse it altogether without even trying it. These people are more likely to be open to a surgical option."

Inspire's Commercial Expansion Initiative

- "Inspire has specific criteria—not everyone is eligible. The main criteria is based on a diagnostic tool to assess OSA severity, whereas five to 15 apneas per hour is considered mild, 15 to 30 apneas per hour is considered moderate, 30 to 80 apneas per hour is considered severe, and more than 80 is considered super severe. Inspire criteria is 15 to 65 apneas per hour. Other exclusion criteria are severe obesity and upper airway obstruction, which can be determined by a drug-induced sleep endoscopy test to observe how the upper windpipe closes. If the closure is anterior/posterior, the patient is eligible for Inspire. A concentric collapse is exclusionary."
- "Although CPAP intolerance appears to be a growing concern, the rate is more a reflection of a broken medical system than a flaw in the technology. Until very recently, most patients would be referred for a sleep study by their primary care physician. When diagnosed with OSA, in many instances by a remote pulmonologist, the primary care physician would then prescribe CPAP. The device is provided by a durable medical equipment company but the patient commonly received no real training, guidance, or support. So, out of frustration, a lot of CPAP machines end up in the garage or under the bed. This is why the market for CPAP options has flourished."

- "With more facilities and practitioners specializing in sleep medicine, the situation is much improved. Many times, new CPAP patients simply need a little handholding. I can only hope that with better care the percentage of CPAP success will increase. Based on my experience, true CPAP intolerance/failure is much less than 35%."
- "Ultimately, CPAP is an adjustment and it is not the most sexy thing in the world but it is the least invasive, which is appealing. It also looks scary and makes a poor impression on patients, but the new CPAP masks are much more comfortable. I think we will continue to see advances with CPAP technology that will improve patient experience and help with adoption and compliance."
- "More patients have come to me recently that already know about, and ask for, Inspire. The aggressive direct-to-consumer advertising on the radio appears to be having an effect. It may be the spouse that hears the ad and encourages the patient to explore it. But I always talk through all the options—if I can convince folks to give CPAP a try, I have a lot of success with compliance. But a small percent just do not want to deal with the machine and will consider the surgical option."
- "Other competing technologies include: LivaNova (investigational use only), remedē for central sleep apnea where there is no obstruction but rather faulty signals between the brain and the muscles that control breathing."
- "We will always be looking for alternatives for OSA treatment. Even the small percentage of CPAP intolerance equates to a large number of people. Rather than devices, the more interesting area is pharmaceuticals. There are ongoing studies now with a combination of oxybutynin [a urinary incontinence medication] and atomoxetine [and ADHD medication] which seems promising. A pharmaceutical option would be a more reasonable option for many OSA patients."

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Physician with a West Coast university-based sleep medicine department

Inspire's Treatment

- "Although a last resort option for my patients, those who have undergone the procedure are generally satisfied."

3) Owner of a CPAP alternative sleep center in the Southwest

This source focuses on CPAP alternatives, primarily oral appliances, which have been categorized as an acceptable first-line therapy for mild to moderate OSA, although criteria and coverage varies by insurer. Sleep doctors generally have a financial interest in both the sleep center and the DME, which provides further incentive for them to automatically prescribe CPAP to new OSA patients. The CPAP failure rate is closer to 60%. The high failure rates can be attributed to the lack of patient education and unexpected consumable/maintenance requirements. This source has limited interaction with Inspire patients but those she has spoken with claim a high level of satisfaction. Of the failed Inspire consultation patients she sees, 50% fail because they do not meet the medical criteria and 50% fail due to fear of surgery. Patients most likely to pursue Inspire are those who have tried everything and are desperate for OSA resolution and those who are drawn to a quick, surgical fix, although this source could not estimate the size of these groups. DTC advertising has not been successful for the oral appliance industry, primarily as a result of variable coverage. If Inspire is well covered they may fare better. A pharmaceutical for OSA may be very appealing to many people.

Background

- "My sleep center specializes in oral appliance therapy. Medical guidelines categorize OSA diagnoses as mild, moderate, or severe. First-line therapy can be either CPAP or oral appliance for mild or moderate, according to patient choice. Previously, appliances were a second-line option for CPAP failures."

Inspire's Commercial Expansion Initiative

- "My experience in speaking with patients is CPAP failure is closer to 60%. OSA is a lifetime diagnosis—it does not go away. Almost everyone diagnosed with OSA is still prescribed CPAP first, even though appliances are the least invasive."
- "Follow the money. The sleep doctors have a financial interest in both the sleep center as well as the durable medical equipment company. As such, these doctors are motivated to prescribe CPAP first; most patients do not get alternatives. Once diagnosed, a patient gets a CPAP sent to their house. Integrating the device into lifestyle is tough without guidance or education. Some are also surprised by the CPAP consumable expenses and maintenance."

- "If you survey most sleep doctors, they know for a fact the CPAP works but the factor that is not always considered is the patient. Will they use it? I consult with newly diagnosed OSA patients. Nine times out of 10 they don't know what OSA is, how it affects their health, and what their sleep study findings show. No one had taken the time to have the conversation. The turn-around pressure at a sleep center does not allow for proper education. Providers are so busy checking boxes to ensure they get paid by the insurer that there is no time for patient care."
- "Since dentists have never owned sleep labs, they are not in the loop. Oral appliances for OSA came as a result of device research for TMJ. We are a small group having difficulty getting traction as a routine first-line therapy option."
- "DTC marketing is very common in the oral appliance industry but it has been a failure, in large part due to various insurance criteria and coverage. If Inspire has consistent coverage for their target market, they may fare better."
- "Patients often come to see me for a CPAP alternative but they generally do not understand that there is still a required process, including sleep studies. They can get frustrated. They want a quick fix immediately. It is the Amazon mentality."
- "The patients most likely to explore and succeed with Inspire are those who really suffer and have tried everything [CPAP, oral appliances]. They are desperate because of serious comorbidities and quality of life issues. The other group include those who are drawn by the convenience of a surgical fix. They do not want to deal with a contraption and the maintenance that goes along with it. It is difficult to say how big these populations are."
- "Lifestyle changes would go a long way to resolve OSA prevalence. Obesity is one thing but people are largely unwilling to do the work. Another happens much earlier in life. Bottle feeding has been shown to interrupt natural oral structure development, resulting in OSA even in children. Many of these kids are misdiagnosed. In fact, OSA as a whole is widely under diagnosed. The total affected population is enormous."
- "What Inspire is doing as far as raising OSA awareness is fantastic. More treatment options have got to be a good thing, as one size does not fit all. I am eagerly awaiting an effective pharmaceutical—most people tend to like a solution in pill form."

What Inspire is doing as far as raising OSA awareness is fantastic. More treatment options have got to be a good thing, as one size does not fit all. I am eagerly awaiting an effective pharmaceutical—most people tend to like a solution in pill form.

Owner of a CPAP alternative sleep center in the Southwest

Inspire's Treatment

- "I have spoken with only three Inspire patients. Each were pleased with the results. Most of my patients are failed Inspire consultations due to medical disqualification [50%] or fear of surgery [50%]."

4) Director of sleep educators at a sleep center outside the United States

A failure rate of 30% to 35% for CPAP is a good estimate. Inspire can generally eliminate snoring but may not eliminate the other respiratory events associated with OSA. This source does not consider Inspire as a first-choice CPAP alternative. On the other hand, any form of positive airway pressure will completely eliminate snoring and improving AHI score. For those intolerant to the pressure, this source believes a combination of structural ENT surgery and lower PAP is optimal. Younger people are more likely to opt for a surgical intervention. Because Inspire has strong insurance coverage, there are no significant roadblocks to growth other than the groups of patients who will always refuse surgery. Technological advances in oral appliances are coming and dentists are more involved in treating OSA than they have been.

Inspire's Commercial Expansion Initiative

- "I would agree that 30% to 35% is a good estimate of total CPAP failures, although I honestly think ENT surgeons may offer a lower estimate to defend how effective surgery is as an option. It also depends on the OSA severity. Surgery may bring the more severe cases into the mild range. The Inspire titration generally effectively eliminates the snoring but may not eliminate all of the respiratory events related to OSA."
- "Because Inspire's surgical procedure is covered by most insurers, they have no significant roadblocks to growth—but there will always be a group of patients that will refuse any type of surgical intervention."
- "In my opinion, any form of positive airway pressure [including CPAP, APAP (automatic positive airway pressure), BiPAP (bilevel positive airway pressure)] is 100% effective in eliminating both snoring and improving the patient's apnea-hypopnea index. The challenge lies with those who are intolerant to high pressure. In these instances, I

believe a combination of ENT surgery [e.g., tonsillectomy if appropriate] and lower PAP pressures would be most beneficial."

- "Other CPAP alternatives include auto-PAP, bilevel, and oral appliances [e.g., mandibular advancement devices]. Dentists are becoming more involved in treating OSA and more technological advances are in the works. CPAP itself has also evolved—it was originally developed in the early 1980s. Prior to that, tracheostomy was the only treatment."
- "Technology success is closely related to severity. From my own experience, moderate to severe OSA greatly benefits from PAP therapy. Those in the milder range, as well as younger patients, may equally benefit from surgical technologies or oral/dental devices."

Inspire's Treatment

- "Younger people are more likely to opt for surgery vs. dealing with the CPAP machine. But surgery is not without some lifestyle accommodations. For instance, Inspire patients are encouraged to sleep on their sides, whereas with CPAP one can sleep in any position as long as optimal pressure has been obtained."

> **Because Inspire's surgical procedure is covered by most insurers, they have no significant roadblocks to growth—but there will always be a group of patients that will refuse any type of surgical intervention.**
>
> *Director of sleep educators at a sleep center outside the United States*

5) Director of a sleep center for 11 years in the Northeast

This center's patient load is well controlled with CPAP and this therapy is well tolerated by almost all of its patients. The center does not see patients who would be candidates for Inspire therapy. Those patients would be treated in the local university hospital but it is not an issue raised by their patients or initiated by their practice. This clinic is not referring to Inspire centers due to low numbers of failures or treatment intolerance.

Background

- "We are a busy sleep center, doing sleep studies, diagnosing sleep apnea, prescribing appropriate therapy, and controlling patients' obstructive sleep apnea. We see very few patients who fail and who need alternative treatments like Inspire. Our patients are professionally managed on CPAP therapy. Our healthcare professionals do not do these other types of procedures. I know where these procedures can be performed—the university hospital or Meridian Hospital—but we do not see patients who need these procedures."
- "Our patients get good results from CPAP and tolerate this therapy well. Patients seldom raise the issue of alternative therapies or Inspire. We are not referring patients to these Inspire centers."

Inspire's Commercial Expansion Initiative

- Did not discuss.

Inspire's Treatment

- Did not discuss.

3) Sleep Apnea Device Sales Channel

Inspire's published TAM is considered accurate or even understated, according to these four sales professionals working in the sleep apnea space. All four expect continued growth and increased adoption of Inspire's treatment by patients that fail or cannot tolerate CPAP. However, one source said until COVID-19 is less prevalent, Inspire's growth will not be significant. The primary headwinds Inspire must address to drive growth include the lack of patient and physician awareness of its OSA treatment and sleep centers' unwillingness to inform patients of the treatment option. Sources said sleep centers do not advise patients of the alternative OSA treatments because it would mean the loss of revenue for providing a CPAP solution and the associated consumable income. Two sources said Inspire's promotional efforts are effective and are raising awareness of alternative treatments for sleep apnea. Patients that undergo the Inspire procedure are highly satisfied with the procedure. Nyxoah and LivaNova are considered future competitors if and when they are approved by the FDA. Remedē is not a direct competitor of Inspire OSA treatment device but it is considered an excellent treatment for CSA.

Key Silo Findings

Background

- 4 sources represent competing OSA and CSA treatment products and procedures.

Inspire's Commercial Expansion Initiative

- 4 said Inspire's published TAM is accurate or even understated due to the high incidence of CPAP failure.
- Continued adoption and use of Inspire's therapy are expected. Headwinds include lack of awareness of the procedure and sleep centers' unwillingness to refer patients out of the fear of lost revenue.
- 1 said until COVID-19 is less prevalent there will not be significant growth.

Inspire's Treatment

- Inspire patients have a higher level of satisfaction that CPAP patients.
- Future competition is expected from Nyxoah and LivaNova.

1) Territory manager for implantable sleep apnea device

The Inspire TAM numbers are accurate, according to this veteran medical device industry professional. The market penetration for implantable devices is a mere 1% to 2%, as 9,000 of the 500,000 CPAP failures have undergone the procedure. Future potential is huge. The main headwind for implantable devices is lack of patient knowledge—this source believes 99.5% of patients are not aware of these options and sleep centers and their health care professionals do not inform them. It is not in the best financial interest of sleep centers to refer their patient base away and cut off the revenue stream of follow-up visits and DME sales of CPAP machines and disposables. This is most prevalent with the independent sleep centers. CSA can only be successfully treated by the remedē product by Respicardia and this market is seven to eight times smaller than the OSA market.

Background

- "I sell the remedē product for Respicardia. It is indicated for patients with central sleep apnea or CSA. It is particularly valuable when there is underlying cardiovascular disease, such as diminished ejection fractions of less than 45% and atrial arrythmias like PATs. In many cardiovascular [CV] patients, you do not know what caused what—did the CSA lead to CV disease or did the CV disease cause the CSA? Remedē works by stimulating the phrenic nerve which in turn stimulates the diaphragm to stimulate breathing. The alternative to remedē for CSA would be ASV or adaptive servo ventilator, which will adapt to the breathing pattern real time vs. CPAP, which is constant and does not change. Remedē is typically prescribed and implanted by the cardiologist."

Inspire's Commercial Expansion Initiative

- "The numbers presented by Inspire are pretty accurate, according to my knowledge and what we see in the field. When you look at growth potential with 700,000 CPAP failures and 500,000 implant candidates, only 1% to 2% of the market has been penetrated. The upside is tremendous to grow to a multiple of where it is today."
- "The OSA market is about seven to eight times the size of the CSA market. That means, at 1% to 2% penetration, there is tremendous room for growth for both therapies."
- "About 10% to 20% of patients on CPAP are non-compliers. Combined with failures and other problems, it is about 35% who drop out of therapy. The sleep doctors should be active to treat these patients with alternatives. Too often that doesn't happen."
- "The two main obstacles to growth rates at multiple of the current status are 1. lack of patient knowledge—99.5% do not know of the advances and 2. the resistance of the sleep doctors and the sleep centers."
- "CPAP can treat all OSA, but it does nothing for—and can even hurt—CSA patients. Only remedē can help CSA."
- "The clog in the funnel for an even greater increase in implant-based, non-CPAP therapy is the sleep center/sleep office. They do not seek more aggressive forms of therapy. In independent sleep centers, the [healthcare providers] are typically the DME providers for the CPAPs and the disposables. There is a distinct conflict of interest for them to discontinue the CPAP and refer you to a center for an Inspire or remedē implant. They lose revenue in all ways. ENT and cardiovascular offices are typically motivated for more state-of-the-art therapy."
- "99.5% of OSA or CSA patients get little to no knowledge about alternatives from their sleep doctors. Now Inspire is getting TV and radio spots to stimulate new thinking and motivate patients to discuss this with their sleep doctors. Greater use is all about education."
- "Typical sleep office practice is to diagnose, prescribe a CPAP. If this fails, then try a dental appliance and discuss weight loss and potentially whittle down the choices. They typically don't promote surgical options."

Inspire's Treatment

- "Some patients will reject the implant and not go this route. With OSA and Inspire, there are more options and a greater likelihood—though still small—that a patient will learn about the procedure and reject it. With CSA and remedē there really is no alternative and less likely that will be the reason to reject it."
- "Both Inspire and Respicardia have been doing office promotions and using patient ambassadors and speakers to inform sleep patients of these new options. Inspire has been doing it longer than Respicardia and is better at it. It is an effective way to get more patients aware and in front of their doctors. Both companies are doing more Zoom meetings now and they are effective."
- "I cover most of Ohio and all of West Virginia and Kentucky. There are probably 10 Inspire practices in this geography."
- "Remedē and Inspire are not competitors. Remedē is for CSA and Inspire for OSA."
- "I've heard there is another implantable device in the pipeline that has surgical advantages. You'll have to ask the ENTs about this."
- "Remedē has extremely high patient satisfaction. Most of these patients are desperate for an effective treatment. They have tried the sleep office CPAPs and appliances, etc., but are still not sleeping and often tired all the time. After the remedē procedure—remember, CPAP does not help the CSA cause—their specific issue is addressed for the first time. 90% of patients say it changed their life. [There is an] example last week of a patient who slept 90 minutes a night and was miserable in daytime. [He] got the remedē and, after waiting the recovery period, when it was activated, started sleeping through the night for the first time in years. [The] patient had to be diagnosed but, once identified, it was a life changing event."
- "A big account for Remedē might be two procedures per month. The Ohio State University is an example."

Both Inspire and Respicardia have been doing office promotions and using patient ambassadors and speakers to inform sleep patients of these new options. Inspire has been doing it longer than Respicardia and is better at it. It is an effective way to get more patients aware and in front of their doctors. Both companies are doing more Zoom meetings now and they are effective.

Territory manager for implantable sleep apnea device

2) Sleep apnea treatment territory manager in the Southwest

The potential patient numbers that Inspire has announced match up with territory observations due to CPAP failures and intolerance. Inspire's marketing is prompting obstructive sleep apnea patients to ask their sleep doctors about Inspire and is drawing them into the certified ENT offices to make appointments and learn more about the product. Conflicts can arise for Inspire where the sleep specialty practices own the DME distribution and when the patient is lost to follow-up to the ENT performing the procedure. Patient selectivity is critical, as there are many reasons for sleep disturbances. There is a competitive product one to two years out that reduces the number of incisions and scars during implantation, yet achieves the same outcome.

Background

- Territory manager for a sleep apnea treatment company for more than two years and eight years of experience selling medical devices.

Inspire's Commercial Expansion Initiative

- "The numbers that Inspire has published for OSA patients, numbers on CPAP, percentage of failure and potential for Inspire procedure, seem about right from experience in the field. There are many patients dissatisfied with their therapy that will eventually seek an alternative."
- "The marketing efforts of Inspire are creating awareness and questions that are coming into the sleep doctor's office. The marketing is pulling patients to the Inspire certified offices if the sleep specialists don't bring it up."
- "There are some conflicts of interest in the sleep practices. Some of the practices have ownership in the DME providers and, therefore, have incentive to keep the patients using and purchasing the CPAP devices and disposables. Compounding the potential loss of revenue, if the patient gets the Inspire implant, which is implanted by the Inspire-certified ENT, they typically lose the patient to follow-up and the patient becomes a patient of the ENT. Specialist don't like losing patients to other specialists."

- "Sleep centers are interesting, as well. It is hard to keep a high percentage of patients compliant. I hear that a lot of their patients are lost—just stop the CPAP and do not return to the office. If you ask the practice, they usually don't admit that they have a significant number of patients lost to attrition and don't agree with 35% of patients failing on CPAP."

Inspire's Treatment

- "One of the significant headwinds Inspire fights is patient selection. There are lots of reasons people do not sleep through the night that get diagnosed as obstructive sleep apnea or OSA. Chronic pain patients do not sleep well because they have such a hard time staying comfortable where movement and ensuing pain will awaken them. The Inspire procedure implants a foreign object into their body and many patients with sleep issues feel the implant or worry about 'this thing in my body.' Many take antidepressants and other drugs that can disrupt sleep."
- "There are new drugs coming—a new one was just approved that may be competition for sleep treatments."
- "Respicardia has the remedē implant for central sleep apnea. The criteria for its use are very detailed and narrow. I don't see it used much but it is a viable option for select patients."
- "There is another hypoglossal nerve stimulator one to two years off—still in trials. I've heard its advantage is that there is one less lead going to the epiglottis so that there would be one less incision and scar with this new product. I don't know much more about it."

> **The marketing efforts of Inspire are creating awareness and questions that are coming into the sleep doctor's office. The marketing is pulling patients to the Inspire certified offices if the sleep specialists don't bring it up.**
>
> *Sleep apnea treatment territory manager in the Southwest*

3) Competitive territory manager in the Great Lakes area

The patient numbers Inspire has announced seem about right. Sleep centers state they do not see many failures—not 35%—but centers tend to be "fat, dumb, and ignorant" and end up with patients walking away and finding alternative treatments on their own. There is little holding back the growth of this market other than getting the word out so that patients know there are options other than CPAP.

Background

- "I currently sell the remedē device for management of central sleep apnea. It is an implantable device and the procedures are conducted by cardiologists."
- "Respicardia is a competitor to Inspire. They have been out three years and the reception to the remedē product has been great. It has a narrow indication—a lot of qualifiers before it should be chosen—but is a great alternative for the healthcare professional and the patient."

Inspire's Commercial Expansion Initiative

- "Numbers and potential patients that have been announced by Inspire seem pretty much on target. I do know there are a lot of dissatisfied sleep apnea patients that are looking for alternatives."
- "Regarding headwinds to overcome, when the patient fits the indication for the product, there is very little holding back the use of the products. I don't see much resistance—just a need to get the word out."
- "Insurance coverage and approval is good for this class of treatment. Approvals depend on geography and carrier but, generally, coverage is not a problem."

Inspire's Treatment

- "Sleep centers see most of the patients and many are not happy with the CPAP and the results. If a sleep center says they are not seeing patients dissatisfied with their treatment, they are not paying attention and are fat, dumb, and ignorant to what is going on."

4) ENT sales consultant for an international surgical equipment supplier and former Inspire sales executive

This source has a positive-leaning opinion on Inspire and thinks its total available market to be as large as the company suggests. The market may even be larger, assuming that 80% of potential OSA patients are undiagnosed. This source noted two of Inspire's direct competitors but indicated that the biggest competitive threat is unawareness. Prior to recent

policy reversals, lack of insurance coverage was Inspire's largest obstacle—then COVID-19 hit, reducing surgical operating capacity by 50% across the board. The long-term prospect for Inspire is good but it depends on the course of COVID-19.

Background

- "I was a territory manager for Inspire Medical Systems. I haven't worked with them for a couple years but I keep up with their progress."

Inspire's Commercial Expansion Initiative

- "Inspire's projected total available market seems to align with industry numbers, so I see no reason to believe otherwise."
- "Inspire's TAM is actually larger than presented because 80% of OSA patients are undiagnosed."
- "I consider Nyxoah and LivaNova direct competition to Inspire Medical Systems."
- "Traditional surgery is another competing force, but the biggest competitive threat is unawareness."
- "Prior to recent times, lack of coverage by payers was their largest obstacle, but that's not an impediment now."
- "Once COVID hit, everything slowed down. Sleep centers are operating at 50% capacity. Until COVID loosens its grip, I would not expect significant growth numbers."

> **Once COVID hit, everything slowed down. Sleep centers are operating at 50% capacity. Until COVID loosens its grip, I would not expect significant growth numbers.**
>
> *ENT sales consultant for an international surgical equipment supplier and former Inspire sales executive*

Inspire's Treatment

- "As a prior Inspire sales executive, I am familiar with their surgically implantable device. Patients were generally satisfied with the procedure."
- "Patients who elect for surgery are more satisfied with their treatment compared with traditional CPAP therapy."

4) Industry Specialists

Two of three sleep industry specialists think Inspire's TAM is larger than the company has estimated and increased use of its implantable OSA therapy is likely. One source said Inspire has overstated its TAM and is buying its sales vs. growing organically, implying that it is not a superior technology. Because Inspire therapy requires surgery, it is expected to always be a second-line treatment vs. CPAP. However, Inspire has generated strong clinical trial data from prestigious institutions, secured broad insurance coverage which requires a low copay, and its DTC outreach is driving high levels of patient interest and inquiries. One source said he expects Inspire to generate strong growth for the next five years. The surgery for Inspire is well tolerated and much more appealing that older surgical OSA solutions. Patients that pursue Inspire are highly motivated and consider the treatment life changing. Future competition is expected to come from yet-to-be-FDA-approved Nyxoah, which one source called a "better mouse trap," LivaNova, and, possibly, pharmacology.

Key Silo Findings

Background

- 1 source is an independent sleep consultant.
- 1 source is a Ph.D. clinical scientist and sleep research design and analysis consultant.
- 1 source is a former CEO of a company that produced surgical equipment for surgical procedures for OSA.

Inspire's Commercial Expansion Initiative

- 2 said Inspire has underestimated its TAM and they expect use of its device to grow.
  - 1 said Inspire's clinical trial data, broad insurance coverage, strong clinical education program, and DTC promotions will generate growth for the next 5 years.
  - 1 said Inspire is well established and will be around for the long haul. Its minimally invasive surgical procedure is much more appealing than older procedures.
- 1 said Inspire has overstated its TAM and is buying its sales, implying that its treatment is not superior technology.

Inspire's Treatment

- 3 acknowledge that surgery will always be a second-line treatment for OSA vs. CPAP.
- 1 said the Inspire treatment is well tolerated and life changing for patients.
- 1 said the Inspire patient group is highly motivated for success.
- Future competition is expected from yet-to-be-FDA-approved Nyxoah, LivaNova, and, possibly, pharmaceuticals.

1) Independent sleep consultant

This source believes Inspire's real TAM is higher than the company estimates. Of the 54 million U.S. adults that suffer from sleep apnea, only 20% are diagnosed, but half of those fail CPAP. There are millions of potential customers and, as obesity increases, so will the need for OSA therapies. Many will not want surgery of any kind and some will opt for dental appliances, but there is still a large group who will opt for this technology. They want a quick fix. In this source's experience, the Inspire procedure is well tolerated and life changing. Inspire spent the time and money to pursue peer-to-peer, case-by-case insurance approval prior to formal coverage. Inspire patients never paid much out of pocket. The company also invested in clinical trials at prestigious institutions and clinical education. Inspire is aggressive with new customers, requiring them to share their patient data and purchase a $2,000 device programmer. It pays key opinion leaders well to participate in its Speakers Bureau to gain influence and loyalty. Inspire was a spin-off of a 20-year-old Medtronic technology, but they did it right. This source is 100% certain Inspire will enjoy strong growth over the next five years. Future competitors include Nyxoah and LivaNova.

Background

- Source is a sleep consultant and former sleep lab manager.

Inspire's Commercial Expansion Initiative

- "The latest estimates are that 54 million U.S. adults [more than 30 years old]) suffer from sleep apnea. 80% are undiagnosed. Of the 20% OSA diagnosed patients, 50% are CPAP non-compliant. They just can't use it—positive pressure is uncomfortable and it has to be used whenever the patient is asleep. They get frustrated and throw the device across the room. So, the total CPAP non-compliant market is more along the lines of 5.4 million with a total undiagnosed population of 43.2 million adults."
- "Failing CPAP is the first use criteria for Inspire. Other criteria include weight, upper airway construction/closure, and sleep apnea severity. It is not all that strict. And, although I would expect the majority of candidates to decline because of the required surgery, that still leaves millions of potential Inspire customers."
- "OSA is increasing with the increased prevalence of obesity and that trend is only expected to increase. The problem with sleep apnea is that it doesn't go away and, even if and when people try to lose weight, 95% gain it back in the first year."
- "Many will not want surgery of any kind. Some percentage will opt for oral appliances, but they still have to deal with a device. And, currently, there is no pill to address the root cause of OSA. Available pharmaceuticals only address daytime alertness because these patients have a high risk of falling asleep at work or while driving."
- "Inspire started with a single sleep lab and in five years they have several hundred sleep labs—a number I expect will double in the next five years. Sleep lab closures due to COVID may impact procedures in the short term and, as new, less invasive technologies enter the market, competition will get stiffer. But, in the next five years, Inspire growth should be strong. I am 100% confident that Inspire will grow aggressively for at least the next five years until competition builds awareness and credibility."
- "Inspire has a five-year head start educating physicians. And, although they have been doing radio spots for at least a few years, they have been increasing their DTC efforts through television and social media. This is certainly driving more direct patient interest and inquiry."
- "Inspire clearly understood the need to have insurance reimbursement from the beginning. Their physicians got on the phone with carriers to achieve peer-to-peer approval. They effectively sold the technology based on the upfront cost equating to an overall savings through avoided comorbidities and the lack of resupply and replacement. Even the initial Inspire patients did not have to pay because of this successful peer-to-peer approval process. That set the precedent for more formal approval. If they hadn't done that, no insurance company in the world would have paid based on a routine submission when the cost for CPAP is only about $1,000."

> Inspire started with a single sleep lab and in five years they have several hundred sleep labs—a number I expect will double in the next five years. Sleep lab closures due to COVID may impact procedures in the short term and, as new, less invasive technologies enter the market, competition will get stiffer. But, in the next five years, Inspire growth should be strong. I am 100% confident that Inspire will grow aggressively for at least the next five years until competition builds awareness and credibility.
>
> *Independent sleep consultant*

- "There are not enough sleep clinicians to hand hold patients toward increased CPAP compliance. From the patients' perspective, Inspire is a one-time procedure with a hands-off approach thereafter—it is appealing. They want a quick fix—that's American way."
- "Inspire has been really smart and assertive. They've done it right. They spent the time and money to go through the process of peer-to-peer consultations with the insurers, as well as proper clinical trials with top sleep medicine thought leaders to maximize credibility. The foundational technology was developed 20 years ago at Medtronic. Inspire spun off less than 10 years ago with a team of less than 50 people and one sleep lab. They grew responsibility. There is no smoke and mirrors. They are, however, borderline aggressive. For example, when a physician reaches out to them for information, they demand a lot of patient data and force the sleep center to buy a $2,000 device programmer. They have aggressively pursued private insurers with the peer-reviewed data, education at medical conferences, etc. The one iffy aspect is their practice of paying influential physicians very well to participate in the Inspire Speakers Bureau—one might interpret that as buying influence and loyalty."
- "Nyxoah is a less invasive procedure and may prove to be a formidable competitor down the road. It is currently approved in the EU and the company is actively seeking FDA approval. They are already starting to build a sales team in the U.S. An additional advantage is that Nyxoah has no implantable power supply, whereas Inspire's battery has to be replaced every 10 years."
- "There's another hypoglossal nerve stimulator not currently FDA approved: ImThera Medical's Aura 6000 [which was purchased by LivaNova in 2018]. They were doing research in Europe first because of the easier approval process."
- "Remedē is for the more rare central sleep apnea so does not compete with Inspire."

Inspire's Treatment

- "I have talked to people who have had the Inspire procedure/titration. They all claim that the surgery was not that bad and that the technology has saved their lives. Down to a person, each will state how fortunate they are to have the Inspire option because they could not tolerate CPAP."

2) Ph.D., clinical scientist, and sleep research design and analysis consultant

This source states that published data on CPAP adherence ranges from 30% to 60%, so Inspire's TAM estimate for CPAP failures is probably low. Much of this failure is likely due to poor patient education. OSA is a very heterogenous population and much of the detail is just coming to light. The ideal patient for Inspire is one with tongue obstruction, but patients with other underlying causes are less likely to be good candidates. OSA patients who opt for surgery are a self-selected group. They want a quick fix/cure and are highly motivated for success. They want it to work. But surgical interventions will always be a second-line therapy. This source describes possible future OSA therapy alternatives in negative pressure technologies and pharmaceuticals. Inspire has established itself and should be around for the long haul.

Background

- This source is a sleep research consultant and former academic sleep researcher.

Inspire's Commercial Expansion Initiative

- "The available market depends on how you define CPAP failure. [The Centers for Medicare and Medicaid Services] defines adherence as use for less than four hours each night 70% of the time [seven out of 10 nights]—but this is not data driven. It is completely arbitrary but became set in stone. No one thinks the low end of the adherence reflects adequate treatment. What happens practically is you get people who can adapt and use it very consistently [seven or more hours a night, seven nights a week] and the other end the spectrum with people who struggle and eventually fail entirely. CPAP adherence rates range from 30% to 60% in the literature, so an estimate of 35% failure is probably low."
- "CPAP failures involve mask fitting, equipment, pressure [APAP v. CPAP], and general ignorance of the patient's own disease and how to use CPAP. Sleep centers don't get paid for educating new PAP patients—they only get reimbursed for the sleep study. Patients get handed off to a durable medical equipment company that has no specialty knowledge and, if not explained and fit well, success rates are low. It is a huge breakdown in the system. Many studies have shown proper PAP education and early check-ins have a monumental impact on success rates."
- "OSA is a very heterogeneous population. Three main types based on presentation are those who are: 1. extremely sleepy, 2. cannot sleep/suffer frequent disrupted sleep, 3. spouse complaints of snoring but patients believe they are asymptomatic. The sleepy respond well to CPAP. Insomnia patients will struggle with the physical burden of CPAP. And the snorers are a grab bag."

- "Identifying an optimal OSA therapy depends on where the obstruction is occurring—big tongue, fatty neck, tonsil obstruction, restricted airway, etc. CPAP is agnostic. Pressure splints the airway open and pushes everything out of the way. This is one of the reasons it is a first-line therapy: it should work for anyone so there is no need to target treatment for the specific patient."
- "Patients who undergo surgical interventions which involve tissue trimming cannot supplement with CPAP therapy because pressure will not be optimal. The same is likely true for Inspire, whereas the hypoglossal stimulation pushes the tongue forward, which would create a pathway for air to escape and could make supplemental CPAP ineffective and/or problematic [swallowing air]."
- "Any kind of surgical procedure is a big undertaking. Patients really want it to work and are mentally convinced that it will. Older surgical interventions were very painful and aggressive, so the Inspire technology offers a much more appealing alternative to the surgical fix. But CPAP will always be first-line therapy. Reputable surgeons will insist on CPAP failure first."
- "Patients want a quick fix. Those opting for surgery are a self-selected group who want the easiest and most permanent 'cure.' CPAP is an effective therapy, but it is not a cure. And never underestimate how vain people are—CPAP is not sexy."
- "There have been a number of companies that have tried negative pressure technologies for OSA but failed. The concept, however, makes sense."
- "I have been hearing about pharmaceuticals for OSA. The therapy probably has to do with the arousal threshold component and perhaps muscle rigidity to keep the airway open. I am not aware of anything specifically available on the market at this time, however."

Inspire's Treatment

- "Inspire has been around long enough that they have proven their mettle and should be around for the long haul."
- "Inspire is a second-line therapy, but it is difficult to figure out who will respond optimally. The more airway is visible, the less likely Inspire will work [because tongue obstruction is not the problem]. As we gain a greater understanding of the underlying causes [including subcategories on the physiological level: pressure tolerance, arousal threshold, etc.], it will get easier to target the most successful therapy. The people with tongue obstructions would likely fall into the Inspire camp. But we are just beginning to understand the different physiological 'buckets' and have no idea what percentage of OSA sufferers fall into each."
- "Inspire may reduce apneic events and lower AHI score but the patient still may have significant sleep apnea. Additionally, if a patient has long apneic events, their AHI score will be misleadingly low because of the calculation. AHI [reduction] does not always tell the story but surgeons rely on it to assess success. Sleep medicine professionals tend to be more holistic when assessing success, including factors such as oxygen saturation, arousal, daytime alertness, and other factors in addition to AHI score."

> **Inspire has been around long enough that they have proven their mettle and should be around for the long haul.**
>
> *Ph.D., clinical scientist, and sleep research design and analysis consultant*

3) Former CEO of a company that produced surgical equipment for surgical procedures for OSA

Inspire's TAM estimate is too high. All companies in this space overestimate the opportunity. People who need CPAP to be functional will use it. Mild OSA patients will not use CPAP consistently but will not opt for surgery, either. The target group for Inspire are those who are not sleeping well, are concerned about their health, and will not use CPAP. This is a much lower percentage than 35%. CPAP has very robust data to support the efficacy of their technology and the manufacturers continue to improve the ease of use/mask comfort. Insurance coverage is vital to success but, even when a new, more expensive technology does get reimbursement, insurers have been known to dial back coverage if it becomes more popular than expected. Moreover, consumers are reluctant to pay out of pocket. This source discussed two OSA technologies (one device and one surgical procedure) that are defunct and Nyxoah, with its implantable technology similar to Inspire, describing it as a better mouse trap. Direct-to-consumer marketing is an interesting model but can be difficult if patients must fail first with CPAP. ENT surgeons must also be educated/trained in order to expand availability/use. This source described early Inspire adopters' experience with procedural difficulty and significant blood loss. It appears to him that Inspire is buying their sales rather than growing organically as a superior technology.

Inspire's Commercial Expansion Initiative

- "The TAM estimations for real CPAP failures/opportunity for alternative technologies are always too high. I have not seen any company achieve them. Some of the problem lies in defining the target market. When one claims 35% of CPAP patients fail, what does that mean? Is it a matter of patients being able to use the machine, but do not? Or does it refer to people who truly cannot use/tolerate CPAP—which is a much smaller percentage. Then you have to look at severity. Severe sufferers will use CPAP. Mild sufferers will not use CPAP consistently and they will not opt for surgery. The people that are in the middle are the real target for a CPAP alternative. The target group are those who are not sleeping well, are worried about their health, and find CPAP too cumbersome/inconvenient. The question is how many of those will opt for a surgical procedure."
- "I have never believed there is strong evidence to suggest a severe OSA sufferer will not comply with CPAP. People that really need it to be functional will use it."
- "CPAP has enough clinical evidence to fill a 2,500-square-foot house. The manufacturers invest heavily and continue to innovate for improved compliance."
- "The clinical data for Inspire's technology is not nearly as good as the data on CPAP. To Inspire's credit, they spent a lot of years and money to get where they are. I am shocked they got this far and achieved $195 a share. But I am suspect of the numbers. They have a lot of cash but I have seen similar profit and loss statements and it usually does not bode well. It seems as if they are buying their sales."
- "Third-party coverage is vital. Ventus Medical spent a lot of time and money to get insurers on board but the carriers started doing the math and the technology never did get covered. From a payer's perspective, they may approve a new technology assuming it will not become pervasive. But, if they miscalculate and a new, more expensive technology does become very popular, they will back off the coverage. This is the very situation that happened in the diabetes market. Significant drops in coverage forced Bayer [AG/BAYRY] and Johnson & Johnson [JNJ] to abandon their diabetes divisions altogether."
- "Consumers are generally not willing to pay much out of pocket, so I assume the Inspire coverage is pretty comprehensive."
- "As far as non-CPAP alternatives, excluding dental appliances, Theravent, formerly Ventus Medical, [last owned by Provent Sleep Therapy LLC] offered a disposable, over the nose medical device for OSA. The technology worked, but it was miserable to use. It constricted breathing. The company discontinued manufacturing in June 2020."
- "Another surgical procedure consisted of four implants in the tongue [a 15-minute outpatient procedure with a one- to three-day recovery]. The implants were designed to provide a light spring-like force to the tongue tissue. After the implants heal into place with the looped ends acting as an anchoring mechanism, the bio-absorbable sections between the looped ends of the implants erode, allowing the implants to gently contract over time. It was a simple procedure, but expensive [at $3,000] without insurance coverage. Also, the complexity of positioning accuracy impacted efficacy. The technology was not ready for prime time."

> **Nyxoah, which I believe is an Israeli company headquartered in Belgium, has an implantable technology similar to Inspire. But it is smaller, simpler—a better mouse trap.**
>
> *Former CEO of a company that produced surgical equipment for surgical procedures for OSA*

- "Nyxoah, which I believe is an Israeli company headquartered in Belgium, has an implantable technology similar to Inspire. But it is smaller, simpler—a better mouse trap."
- "The direct-to-consumer marketing is an interesting model but can be a difficult one. If CPAP is a required first-line therapy, then the patient must fail CPAP first before they are covered for an alternative. The other challenge is what type and what percentage of physicians are aware of the technology. Many OSA patients are referred by primary care, then they may be seen by an airway specialist, but the awareness and training must reach the ENT surgeon."

Inspire's Treatment

- "The Inspire procedure is a long and tough surgery for hypoglossal nerve stimulation. Some years back I remember complaints about a lot of blood loss."

Miscellaneous

- "Most obstructive sleep apnea can be completely resolved by losing weight. But people are looking for an easier fix."

Secondary Sources

These five secondary sources focused on new Inspire treatment center openings, a competitor's fist successful U.S. trial device implementation, and Inspire's implementation into the German healthcare reimbursement system.

Dec.-Nov. New Inspire Treatment Center Announcements

Inspire is aggressively opening new Inspire treatment centers. Each time they do, news outlets publish the new treatment option and, frequently, the new center offers patient education programs to introduce the procedure.

Dec. 1 Newswire article

- "Southern California Pulmonary and Sleep Disorders Medical Center launches Inspire Upper Airway Stimulation therapy, a treatment option for sleep apnea. Inspire works from inside the body with the patient's natural breathing process."
- "A new obstructive sleep apnea treatment called Inspire Upper Airway Stimulation has been launched by the Southern California Pulmonary and Sleep disorders Medical Center in Thousand Oaks California. The treatment is an alternative to Continuous Positive Airway Pressure treatment."
- "More information is available at: https://sleepmd4u.com."

Nov. 25 County 10 article

- "There's a new treatment available for people who cannot tolerate this machine. Specially trained physicians implant a small device that stimulates the upper airway to facilitate breathing during sleep. Experts at St. John's Health will be available to help you learn about this new treatment, called Inspire, during a Virtual Community Health Talk on Tuesday, December 8 at 6 pm."
- "'This new treatment has high patient satisfaction rates, creating a real game-changer for people with sleep apnea,' said St. John's ear, nose, throat specialist Martin Trott, MD, the surgeon who implants the device."

Nov. 8 Hill Country Community Journal article

- "Peterson Health has started offering a new procedure to stop patients' snoring and irregular night breathing associated with "apnea."
- "A small device called "The Inspire" by its manufacturer, similar to a pacemaker, is inserted into the patient's chest, under the skin."
- "The hope is that this device – or 'gadget' as Dr. Sylvester Ramirez, M.D., called it – will replace the standard CPAP appliance, officially a 'Continuous Positive Airway Pressure' machine."

Nov. 17 Medical Device Israel article

After receiving FDA IDE (investigational device exemption) approval in June 2020, Nyxoah announced the successful implantation of the first patient in the DREAM US pivotal trial.

- "Nyxoah S.A. (EBR: NYXH) ("Nyxoah" or the "Company"), a health-technology company focused on the development and commercialization of innovative solutions and services to treat sleep disordered breathing conditions, today announces the successful implantation of the first patient in the DREAM US pivotal FDA study. The implantation took place at Hollywood Private Hospital in Perth, Australia and was performed by Dr. Richard Lewis, MBBS, FRACS, Head & Neck Surgeon."
- "The DREAM (Dual-sided Hypoglossal neRvE stimulAtion for the treatMent of Obstructive Sleep Apnea) study is a pivotal, Investigational Device Exemption (IDE) trial designed to support the marketing authorization of the Genio® system in the United States. This multicenter, prospective, open-label, observational study will enroll 134 patients, who will undergo the implantation procedure in up to 26 centers worldwide including sites in the United States, Germany, Belgium and Australia."
- "Dr. Richard Lewis, implanting surgeon from Hollywood Private Hospital commented: 'Our center has an extensive historical collaboration with Nyxoah. We took part in the BLAST OSA study that led to CE Mark approval of the Genio® system and we are the lead investigator center in the ongoing BETTER SLEEP study testing the effectiveness of hypoglossal nerve stimulation on Complete Concentric Collapse (CCC) patients who are currently excluded from this type of therapy. We are excited to be part of the DREAM IDE pivotal trial together with US and European

physicians and are thrilled to build further clinical evidence on the Genio® system giving more patients across the globe access to this innovative OSA therapy.'"

- "Olivier Taelman, Chief Executive Officer of Nyxoah, added: 'The United States are the largest market in the world for the treatment of patients suffering from Obstructive Sleep Apnea. The DREAM study is designed to support the U.S. introduction of the Genio® system. Enabling US physicians to build their first experience with the Genio® system, combined with the knowledge of other already experienced international surgeons, is supporting Nyxoah's mission to offer its disruptive therapy to more OSA patients around the world.'"

Nov. 9 BioSpace article

Inspire treatment becomes part of routine clinical practice in Germany.

- "Inspire Medical Systems Inc. (NYSE: INSP) ("Inspire"), a medical technology company focused on the development and commercialization of innovative and minimally invasive solutions for patients with obstructive sleep apnea ("OSA"), today announced that Inspire therapy will be integrated into the German hospital reimbursement system ("G-DRG"), effective January 1, 2021. Germany's Institute for the Hospital Remuneration System ("InEK") recently published the list of treatment methods, including Inspire therapy, to be included in the regular DRG catalog."
- "Since January 2016, Germany's reimbursement for the Inspire procedure has been provided through the NUB process for new diagnostic and treatment procedures. The NUB process allows hospitals to submit requests for reimbursement of 'new and innovative treatment methods' that have not yet obtained a G-DRG code. The NUB process requires hospitals to submit applications annually to obtain approval to perform the Inspire procedure. While Inspire therapy has received the top NUB1 rating for each of the last five years, this remains an interim step in establishing formal reimbursement in Germany."
- "'We are very excited to announce the InEK decision, as it will secure long-term reimbursement for Inspire therapy in Germany, which we expect will improve access for patients with untreated OSA in that country. The decision to include Inspire in the DRG catalog demonstrates that our procedure has become part of routine clinical practice in Germany,' commented Inspire President and CEO Timothy P. Herbert. 'Our focus remains on ensuring high-quality patient care with trained centers in Germany.'"
- "Andreas Henke, Inspire's Senior Vice President for Europe, added: 'The decision of the InEK is based on the excellent work of the surgeons and hospitals in Germany who have treated patients with Inspire therapy over the past five years. Their experience with Inspire therapy during this time has shown that a new treatment procedure can be introduced safely and effectively from clinical development to routine care. In fact, the data generated to date from commercial Inspire therapy cases in Germany has demonstrated that our technology has delivered treatment outcomes that are the same or better than the results achieved in controlled studies.'"

Additional research by James Boland, Pam Conboy, and Shane Podolsky.