What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

iSGS Research Highlights – 2025

2025 has been an unusually productive year for idiopathic subglottic stenosis (iSGS) research. Studies published this year have expanded understanding of how the **disease behaves over time**, how pregnancy and **hormones influence recurrence**, which treatments offer **greater durability**, and - critically - what is happening at a **cellular and molecular level** within the subglottis.

This summary distils key peer-reviewed findings from 2025 into clear "What we learned" and "What this means" sections, aimed at helping patients, clinicians, and researchers interpret how new evidence may influence care, expectations, and future research directions.

The research this year tells a coherent story about iSGS:

- iSGS is **biologically distinct**, not simply scar tissue.
- Disease **behaviour declares itself early**, often within the first two years.
- For many patients, durability can be improved **without escalation to open surgery**.
- Hormones matter - but their **role is complex and indirect**.
- Biological stratification of iSGS is no longer theoretical; it is **actively emerging.**

What we learned

1. In-office awake dilation is a safe management option for subglottic stenosis

Reading:
In-Office Balloon Dilation for Idiopathic Subglottic Stenosis: A Pilot Study
Catherine F. Roy, MD et al
https://doi.org/10.1177/19160216251314764

This pilot study looked at whether balloon dilation for iSGS can be safely and effectively done in the clinic under local anaesthetic, rather than in the operating theatre under general anaesthetic.

Eleven patients with an average of 40% stenosis had the procedure. Across the group, breathing symptoms improved significantly, voice scores improved, airway narrowing reduced from an average of 40% to 10%, and peak flow increased from 62% to 99%.

Patients generally returned to normal activities within a day, reported low pain scores, and no serious complications. Among those who had previously had operating-theatre procedures, all preferred the in-office approach because it was quicker, less stressful, and came with a faster recovery.

What this means

For people with mild to moderate iSGS, **in-office balloon dilation** could be a safe, effective, and **far more convenient alternative** to hospital-based surgery.

It may help reduce the burden of repeated general anaesthetics, offer quicker recovery, and make timely treatment easier. While not everyone will be suitable (e.g. those with more severe stenosis or certain other medical conditions) the results are encouraging.

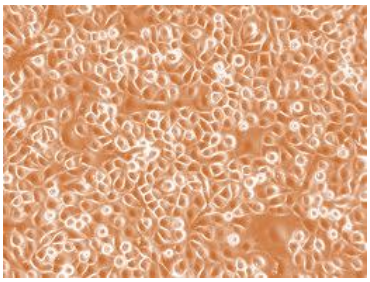
For selected patients, awake balloon dilation may provide meaningful symptom relief with **minimal downtime** and could become an important option in ongoing care

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

What we learned

2.Unique cell populations identified in the subglottis



Reading:
"Cellular blueprint of healthy and diseased human epiglottis and subglottis - a study of the Canadian Airways Research (CARE) group"
Peter Y F Zeng, R Jun Lin et al

https://doi.org/10.1016/j.ebiom.2025.105631

Researchers discovered that the subglottis contains **unique cell populations** not found elsewhere in the airway, which may explain why fibrosis occurs there. In iSGS, they found a shift towards **inflammatory, hormone-responsive secretory cells** and expansion of **fibroblast populations** linked to scarring.

They also identified four molecular subtypes of iSGS ("SUBSET 1–4"), with SUBSET 3 and 4 associated with a **significantly higher rate** of needing **repeat procedures**.

The study also showed a patient's tissue type can **change over time** and identified possible drug classes that might reverse the fibrotic process.

What this means

The discovery of four molecular subtypes could **eventually help predict which patients are more likely to need frequent interventions**, and guide more personalised treatment.

Identifying drug classes that could potentially reverse fibrosis lays early groundwork for **future non-surgical therapies.**

While clinical trials are still needed, this study brings iSGS research a **major step closer to precision medicine**.

What we learned

3. Comprehensive profiling sharpens the biological picture of iSGS

Reading:
"Cohort-level clinical trajectory and molecular landscape of iSGS for precision laryngology – a study of the Canadian Airways Research (CARE) Group"
R Jun Lin et al
https://doi.org/10.1016/j.ebiom.2025.105629

This study followed 126 people with iSGS and combined their clinical histories, biopsy results, and genetic data to understand why the disease develops and why it behaves so differently between patients.

On average, people needed just over one dilation per year, and worse narrowing and older age at diagnosis were linked to more frequent procedures.

Researchers confirmed that the disease is **strictly limited to the subglottis**, with no detectable molecular changes in the nearby epiglottis.

They also identified specific **cell subsets** associated with **more aggressive disease** and found that patients with iSGS tended to have **lower genetically predicted testosterone levels**, providing a potential biological explanation for the strong female predominance.

What this means

This study offers clearer answers about how the disease behaves and why it affects certain individuals. By showing iSGS is rooted in changes within the subglottis alone - not the entire upper airway - it **sharpens the focus for future treatments**.

The identification of cell types linked to a faster recurrence rate may eventually help predict who is likely to need more frequent procedures, opening the door to a more **personalised approach** to care.

The finding of lower genetically predicted testosterone levels also strengthens the theory that **hormonal factors contribute to iSGS**, which may guide new avenues for research.

Overall, this study deepens scientific understanding of the disease, highlights important biological clues, and lays groundwork for **precision laryngology**, where treatment strategies are **tailored to each patient's clinical and molecular** profile.

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

What we learned

4. Pregnancy increases likelihood of stenosis return, but balloon dilation and laser wedge dilation are safe surgical options

Reading:

"Surgical Management of Idiopathic Subglottic Stenosis During Pregnancy: A Multi-Institutional Study" Andrew S Awadallah et al
The Laryngoscope, 2025; 0:1–7
https://doi.org/10.1002/lary.32464

"Pregnancy and Parity as Risk Factors for Recurrence in Idiopathic Subglottic Stenosis" Andrew S Awadallah et al
Otolaryngology - Head and Neck Surgery 2025, Vol. 00(00) 1–6
https://doi.org/10.1002/ohn.1255

Together, these two new studies show that pregnancy has a meaningful impact on iSGS.

The first found that those who had been pregnant **experienced 2.6 times more recurrences than those who had never been pregnant**, even after adjusting for age and follow-up time.

Each additional pregnancy was linked to roughly one extra iSGS recurrence but did not make the time between surgeries noticeably shorter.

The second study found that **endoscopic procedures** such as balloon dilation and laser wedge excision were **safe and effective**, including in higher-risk pregnancies (twins, advanced maternal age, multiple surgeries).

Most procedures were done in the **second trimester**, and there were **no surgical or postpartum complications** related to the airway treatment.

What this means

Pregnancy is a period of heightened vulnerability for people with iSGS - likely due to hormonal changes (very high estrogen and progesterone levels) and increased reflux, both of which may worsen scarring.

For those planning a family, pregnancy can increase the likelihood of needing additional procedures, though it does not necessarily make stenosis return more quickly afterwards. Importantly, if symptoms do flare during pregnancy, the evidence shows that surgery is typically safe for both mother and baby when carried out with specialist teams and foetal monitoring.

Some patients with milder symptoms can safely defer surgery until after delivery.

Overall, these findings support **early, open discussions with clinicians** about family planning, monitoring during pregnancy, and **personalised decisions** on when and how to treat airway symptoms.

What we learned

5. Following a dilation with in-office steroid injections (SILSI) improves the time between surgeries

Reading:

"Surgical Recurrence Across Endoscopic Surgical Techniques in Idiopathic Subglottic Stenosis" Andrew Jay Bowen et al
The Laryngoscope, 2025; 0:1–7
https://doi.org/10.1002/lary.32181

This study compared three endoscopic approaches for iSGS:

- endoscopic dilation (ED)
- laser wedge excision (LWE), and
- ED combined with serial intralesional steroid injections (ED + SILSI) – with all analyses starting from patients' very first surgery.

The results showed that ED had the highest recurrence rate (91%), while LWE (49%) and ED + SILSI (21%) had far fewer reoperations.

At 5 years, only 9% of ED patients remained surgery-free, compared with 54% after LWE and 81% after ED + SILSI.

What this means

Adding **serial steroid injections after dilation** converts ED into a far more durable option - potentially matching or even exceeding LWE in the early years.

Because SILSI is done awake in the clinic, it may offer a **less invasive way to prolong the time** between operations.

The study also highlights the importance of considering factors like age and medical therapy compliance, which influenced outcomes.

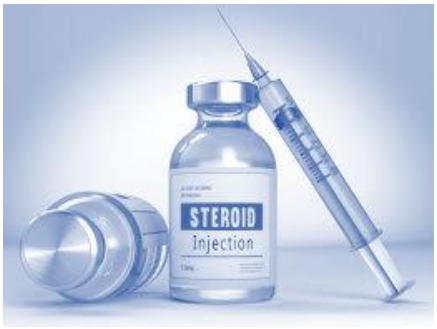
Overall, these findings support a more **personalised surgical strategy**, where patients and clinicians consider not just the immediate result of a procedure, but **how long each technique tends to last** before symptoms return.

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

What we learned

6. SILSI increases surgery-free time for iSGS patients



Reading:
"Effect of Serial Intralesional Steroid Injections on Risk of Recurrence in Idiopathic Subglottic Stenosis"
Shengjie Ying et al
The Laryngoscope, 2025; 0:1–8
https://doi.org/10.1002/lary.32179

This study followed 75 women with iSGS for 1–4 years to understand whether serial intralesional steroid injections (SILSI - in-clinic steroid injections given between dilations) reduce the risk of recurrence.

50% of patients received SILSI and 50% did not.

They found those who received injections remained surgery-free for 2.5 years, compared with 1.4 years for those who did not.

In both single-event and repeated-event analyses, SILSI consistently reduced recurrence risk by about 56–80%, even after accounting for factors like age and time since diagnosis.

What this means

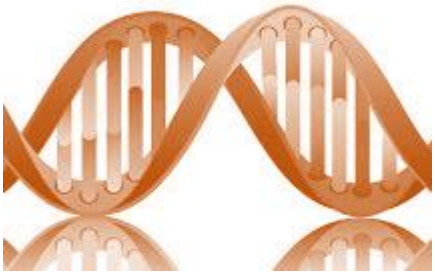
This study provides encouraging evidence that **serial steroid injections** given between surgeries may meaningfully extend the time between procedures. (Also see paper 5).

The authors calculated that for every two patients treated with SILSI, one recurrence could be prevented within two years.

Older age at diagnosis and longer time living with iSGS were also linked to fewer recurrences, suggesting that the **disease may stabilise over time** for some individuals.

What we learned

7. There are differences between the genes in patients with high vs low recurrence rates



Reading:
"Transcriptomic Features of Recurrence Rates in Idiopathic Subglottic Stenosis"
Shengjie Ying et al
The Laryngoscope, 2025; 0:1–7
https://doi.org/10.1002/lary.32214

Researchers analysed tissue samples to measure gene activity. They compared patients with the highest recurrence rates to those with the lowest recurrence rates.

High recurrence patients (dilation every 6-10 months): Showed increased activity of genes related to the immune system (especially B cells) and to scar tissue formation.

Low recurrence patients (dilation every ~18 months to several years): Showed higher activity of genes related to cilia (tiny hair-like structures in the airway that help clear mucus and protect the airway).

What this means

Patients with **frequent recurrence** may have an **immune-driven scar-forming process** that contributes to airway narrowing.

Patients with **less recurrence seem to retain more healthy airway cilia**, which may protect against disease progression.

Understanding these differences could help doctors predict which patients are likely to need more frequent treatments and could lead to new therapies targeting immune and fibrotic processes in iSGS.

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

What we learned

8. The first two years after diagnosis help provide clues about your long-term prognosis

Reading:
"Characterizing Disease Severity Through Surgical Recurrence Rates in Idiopathic Subglottic Stenosis"
Andrew Jay Bowen et al
The Laryngoscope, 2025; 0:1–8
https://doi.org/10.1002/lary.32280

This study followed 157 women with iSGS at two major US centres for at least five years after their first endoscopic surgery.

The researchers looked at how often each patient needed surgery in the first two years compared with the next three years and used this to classify disease "severity."

They found:

- *Group A* – 65-70% - slowed down or did not recur over 5 years (2+ years between operations).
- *Group B* – 20% - had steady, persistent recurrence (every 1-2 years), and
- *Group C* – 16-19% - had faster, more aggressive recurrence (every 6-9 months).

Importantly, no patient characteristics helped predict which group someone would fall into. The pattern of recurrence was consistent across both hospitals, even though their surgical techniques and practices differ.

What this means

The **first two years** after diagnosis provide important clues about how someone's **iSGS may behave long-term**.

This helps set expectations for patients and highlights the urgent need for biological markers and better tools to identify, understand, and hopefully treat the more aggressive forms of iSGS. (see paper 7)

What we learned

9. We can expect to see consistency in future research which will make it more easily comparable

Reading:
"Development of a Core Outcome Set for Intervention Studies in Adults with Laryngotracheal Stenosis"
Gemma M Clunie et al
The Laryngoscope, 2025; 135:3756–3765
https://doi.org/10.1002/lary.32262

A major international study with patients, clinicians, and researchers with the aim of identifying the most important elements to measure in studies testing treatments for adults with laryngotracheal stenosis (LTS).

They agreed on seven core outcomes:

- Level of breathlessness
- Ability to produce an audible voice
- Ability to manage/clear mucus
- Ability to eat and drink
- Health-related quality of life
- Emotional and mental health symptoms
- Frequency of treatment

What this means

Using these seven outcomes in all studies will make **research results easier to compare and combine**.

It ensures studies measure what really matters to patients, not just clinical or surgical results.

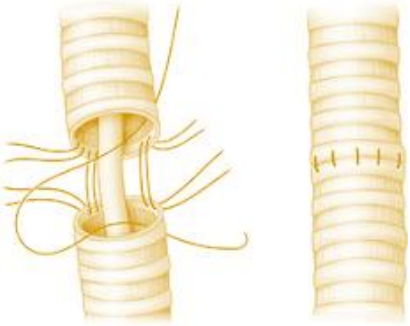
Future work will focus on the **best ways to measure these outcomes** reliably.

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

What we learned

10. Cricotracheal resection remains a long-term solution (not cure) for iSGS



Reading:
"Update of Long-Term Outcomes After Cricotracheal Resection for Idiopathic Subglottic Stenosis"
Breanne L. Schiffer et al
The Laryngoscope, 2025; 0:1–5
https://doi.org/10.1002/lary.32326

This study from the University of Utah examined how well cricotracheal resection (CTR) holds up over decades in people with iSGS – adding 7 years of follow-up to their 2018 report.

In total, 61 patients underwent CTR between 1999 and 2017. The results show that CTR is highly durable for many people: 67% had not experienced any recurrence up to 17-22 years after surgery.

For those who did recur, the average time to recurrence was 13.8 years, though this varied from less than a year in rare cases to over 16 years.

Importantly, none of the patients who received a voice-sparing variation of CTR experienced a recurrence.

What this means

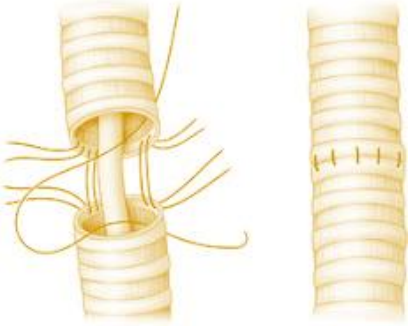
CTR remains the most definitive surgical option for iSGS, and this study strengthens that evidence by showing that **many patients enjoy more than a decade of stable breathing** after the operation.

At the same time, the researchers highlight that **late recurrence does occur**, including more than 15 years after surgery, meaning CTR should **not be viewed as a guaranteed cure**.

Younger patients are more likely to outlive the benefit window, whereas **older patients may be less likely to experience recurrence** or may require fewer procedures if they do.

What we learned

11. Cricotracheal resection is safe when performed at experienced centres (but carries some risks)



Reading:
"Complications following airway resections: Insights from a large contemporary multi-institutional cohort."
Mercier O et al
J Thorac Cardiovasc Surg. 2025 Oct 25.
https://doi:10.1016/j.jtcvs.2025.10.026

Researchers looked at the complications that can occur after airway resection surgery (major open surgery to remove a narrowed segment of the airway and reconnect the healthy ends), with data from 640 adults between 2013 and 2023.

They found that although airway resection is generally safe in **experienced centres**, complications do still happen, particularly issues such as

- breathing difficulties,
- healing problems at the surgical join (anastomosis),
- and infections.

The study also identified patient- and surgery-related factors that make complications more likely.

What this means

This research provides helpful reassurance and transparency for patients considering airway resection.

It shows the surgery is safe when performed in high-volume specialist centres, but it also highlights that risks do exist - and that some people may be more vulnerable to complications than others.

Understanding these risks allows patients and clinicians to have clearer, more realistic discussions when deciding whether surgery is the right option. The findings also support the importance of careful follow-up and **choosing an experienced surgical team**, which can significantly improve outcomes.

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

What we learned

12. The Maddern Procedure can be a viable alternative to open surgery with potentially long-term results

Reading:
Multi-Institutional Endoscopic Resection and Reconstitution for iSGS.
Diana C. Lopez, et al
The Laryngoscope, 2025; 0:1–8
https://doi.org/10.1002/lary.70155

Management of Subglottic Stenosis with the "Maddern Procedure": Long Term Follow-Up Outcomes
Emilie A. C. Dronkers, et al
The Laryngoscope, 2025; 0:1–8
https://doi.org/10.1002/lary.70032

Two major studies - a long-term UK cohort and a multi-centre US group - looked at outcomes of the Maddern procedure (endoscopic resection + mucosal re-lining) for subglottic stenosis, mainly iSGS. Key findings were largely consistent:

- Breathing improved significantly after surgery, with many patients moving to near-normal airflow.
- Surgery-free intervals became much longer - typically several years instead of every few months.
- In iSGS cases, most patients avoided further major airway surgery, with long-term "success" rates around 70–80%
- Outcomes less strong in people who'd had previous open surgery, but many still benefited.
- Mucus issues were common in the first months/years and sometimes needed clinic clean-outs.
- Serious complications were uncommon in specialist centres.

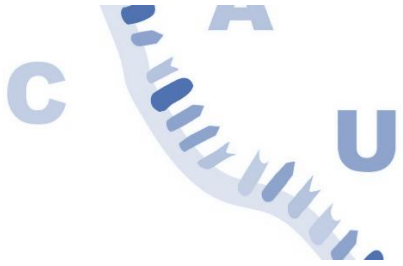
What this means

Taken together, these studies strengthen the evidence that the Maddern approach can offer much longer-lasting relief than repeated dilations alone, without the invasiveness of open reconstruction. It won't suit everyone, and it isn't a guaranteed cure - some people will still recur - but for many, especially with iSGS, it may provide multiple years of stable breathing and reduce the cycle of frequent procedures.

If you're considering your next steps, these findings support discussing the Maddern option with your airway team, ideally in **a centre experienced in the technique.**

What we learned

13. Growing evidence that iSGS has a unique biological fingerprint



Reading:
Multi-Institutional Endoscopic Resection and Reconstitution for iSGS.
Diana C. Lopez, et al
The Laryngoscope, 2025; 0:1–8
https://doi.org/10.1002/lary.70155

Researchers compared airway scar tissue from women with iSGS and women with post-intubation stenosis (iLTS) using RNA sequencing. This allowed them to see which genes and biological pathways were more active in each condition.

They found 68 genes behaving differently between the groups:

- In iSGS, epithelial-mesenchymal transition (EMT) was more active - a process where normal airway lining cells change into a more fibrotic, scar-forming type. This pathway was more active in iSGS than in iLTS, supporting previous research that EMT may be a major driver of

What this means

This study adds to growing evidence that iSGS is **not simply "another type of airway scarring"** but has its own unique biological fingerprint. The stronger EMT signal suggests that iSGS may be driven more by **abnormal behaviour of airway lining cells** rather than by classic inflammation.

This supports the emerging theory that a **weakened airway barrier** may allow irritants or microbes to trigger a **misdirected healing response** - one that leads to fibrosis rather than normal repair.

While this is early-stage (pilot) research, these findings help narrow down specific pathways that could become targets for future treatments, including

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

scarring in iSGS.

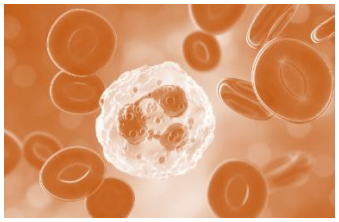
- In contrast, several inflammatory pathways were less active in iSGS than in iLTS, suggesting that the two conditions may be driven by different underlying biology.
- The IL-17 pathway, known to be important in both diseases, came up again as highly relevant
- They also found several cell-adhesion genes and membrane proteins were reduced in iSGS, which may point to a weakened airway lining (epithelial barrier) in iSGS.

therapies that alter EMT, strengthen the airway lining, or modulate IL-17-related immune responses.

It also highlights why iSGS behaves differently from post-intubation stenosis - and why treatments that work for one may not necessarily work for the other.

What we learned

14. CRP cannot predict frequency of iSGS surgery, but a high CRP can mean GPA



Reading:
C-Reactive Protein Serum Values in Idiopathic and Autoimmune Subglottic Stenosis
Andrew J. Neevel, et al
The Laryngoscope, 2025; 0:1–7
https://doi.org/10.1002/lary.70167

Researchers at the University of Michigan reviewed medical records from 106 patients with subglottic stenosis (59 idiopathic iSGS and 47 GPA-related SGS) to see whether a common blood test - C-reactive protein (CRP) - could help distinguish disease type or predict how quickly the airway would narrow again.

They found that mildly raised CRP levels were common in both iSGS and GPA-SGS, but **very high CRP levels occurred only in GPA-related disease**.
Importantly, CRP levels did not correlate with how often patients needed repeat airway surgery (surgery-free interval).

What this means

This study shows that a **single CRP blood test is not useful for predicting disease severity or recurrence** in iSGS. However, **very high CRP levels may raise suspicion for an autoimmune cause like GPA**, which could help doctors decide when more extensive autoimmune testing or rheumatology involvement is needed.

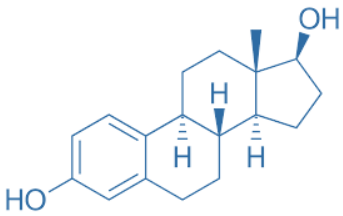
Overall, while CRP reflects inflammation, it **doesn't explain why iSGS behaves aggressively in some patients and remains stable in others**, reinforcing the need for better, more specific biomarkers for airway stenosis in the future.

What did we learn about airway stenosis and its treatment during 2025?

Living with idiopathic subglottic stenosis (iSGS) support community:
www.facebook.com/groups/airwaystenosis

What we learned

15. Estrogen may influence blood vessels and immune cell trafficking



Reading:
The Impact of Estrogen on Stromal Elements in the Proximal Airway in Idiopathic Subglottic Stenosis
Emily L. Mace, et al
The Laryngoscope, 2025; 0:1–8
https://doi.org/10.1002/lary.70216

This study tested whether estrogen (specifically 17β-oestradiol) directly drives scarring in idiopathic subglottic stenosis (iSGS).

Using patient-derived cells, the researchers found that estrogen **did not directly increase fibrosis** in fibroblasts, nor did it worsen epithelial barrier function. Instead, estrogen acted mainly on **endothelial (blood vessel) cells**, increasing angiogenesis (new vessel formation) in iSGS scar tissue.

This suggests estrogen's role in iSGS may be **indirect**, shaping the vascular and immune environment rather than directly causing scar formation.

What this means

This helps refine an important question in iSGS: *why does the disease overwhelmingly affect women?*

The findings suggest estrogen is **not simply "fuelling scar"**, which counters a common fear among patients. Instead, estrogen may influence **blood vessels and immune cell trafficking**, opening the door to more targeted therapies (for example, drugs that affect angiogenesis or endothelial signalling).

While this does **not change treatment today**, it sharpens future research directions and supports the idea that iSGS is a **complex inflammatory-vascular disease**, not just hormone-driven fibrosis.

Prepared by Catherine Anderson, founder of the Living with iSGS support community, December 2025.

Catherine Anderson was diagnosed with idiopathic subglottic stenosis (iSGS) in 2004 following two years of misdiagnosis. Since then, she has undergone more than 25 airway procedures under general anaesthetic and, in recent years, more than 24 procedures while awake under local anaesthetic, receiving treatment in both Australia and the United Kingdom.

*Sixteen years ago, she founded the Facebook-based support group **Living with Idiopathic Subglottic Stenosis** (facebook.com/groups/airwaystenosis). The community has grown to nearly 10,000 members worldwide and serves not only as a peer-support network, but also as a platform for patient education, exchange of clinical experiences, discussion of emerging research, and dissemination of medical literature.*

*Catherine is the author of **The Rough Guide**, a free patient-focused publication that explains iSGS, outlines treatment options, and offers practical advice for daily life with airway stenosis. The guide has been translated into German, Dutch, French, and Spanish and is widely used by patients internationally.*

*Professionally trained in market and social research methods, Catherine combines methodological expertise with lived experience of airway stenosis. As an **independent researcher**, she works collaboratively with clinicians and academic researchers worldwide to design and deliver patient-centred research studies. She is an author or co-author on more than 15 peer-reviewed publications and has contributed to two book chapters.*

*In addition, Catherine is the custodian of an international **airway stenosis patient research panel**, recruited through online communities, patient networks, and clinician referrals. With appropriate ethical approvals, this panel provides researchers with access to thousands of individuals with airway stenosis, supporting timely, inclusive, and high-quality patient-led research.*

*Airway stenosis patients can join the panel by sending an email to: airway.stenosis.research@gmail.com, including their name. **Doctors contact Catherine via**: idiopathic.subglottic.stenosis@gmail.com **to enquire about conducting research.***