

A Bigger Picture Emerges when Patients Lead the Inquiry: Examples from the Cushing's Disease and Syndrome Network

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PURPOSE

Cushing's Support and Research Foundation (CSR) has discussed the impact of persistent high cortisol on long-term quality of life (QoL) throughout its nearly three decades of advocacy as a 501c3 non-profit organization. Our patient community knows they must become experts in this illness because so few providers understand the disease on a deep level. We are encouraged that the FDA and others are embracing rare patient involvement in clinical trial design, drug development, and research because our complex care needs are not fully represented in clinical datasets alone. **Dr. Harvey Cushing, this disease's namesake, famously stated that "A physician is obligated to consider more than a diseased organ, more even than the whole man — he must view the man in his world."**

CSR offers support groups, conferences, a robust website, newsletters, social media outreach, webinars, and other peer programs. In 2019 we began forming occasional focus committees to discuss unmet needs and gaps in care and understanding. We translate the content of these workshops into questionnaires that are shared with our highly motivated membership and often see response rates of 10% or more. The results and response rates of our work attract increasing interest within the professional Cushing's community, and we have collaborated with US and international doctors for comparison studies and exploration of long-term QoL topics. As a non-profit advocacy organization hyperfocused on this patient community and unburdened by institutional regulations and legal department restrictions, we are able to move fairly quickly and collect data from patients around the globe. We believe that we are perfectly positioned to launch a unique global patient registry that will compliment existing institutional registries and the European Register on Cushing's Syndrome (ERCUSYN).

Two major datasets have come out of our committee work since 2020, both largely focused on QoL topics. Initial dissemination of findings is internal, a peer celebration of validation and establishment of commonalities. We have uncovered new statistically significant datapoints to consider when talking about long-term survival and thriving despite such significant challenges.

We will continue to work toward goals that will change the landscape of care, to include:

- Validation of unreported and underreported symptoms and conditions to ensure patients are empowered, educated, and able to advocate for themselves
- Increase in partnerships and collaborations to diversify information and expand support
- Updates to existing QoL and disease-specific screening questionnaires
- Support for new drug and device development
- Creation of a professional platform with IRB oversight to increase patient-provider data sharing
- Regular engagement with the medical community via exhibition, scientific posters, White Papers, and other educational and networking resources

BACKGROUND

Cushing's Disease and Syndrome are caused by persistent high cortisol and can result in a multisystem breakdown that is usually not identified in time to prevent long-term damage. The many non-specific symptoms of Cushing's are fairly prevalent in the US for other reasons and likely impede swift diagnosis: **weight gain, depression, high blood pressure, sudden onset pre-diabetes or worsening of existing diabetes, insomnia, joint pain...**it's a long list.

Cushing's is a rare disease with a prevalence of 5-15 new cases per 1,000,000 residents in the US. Most patients are in their 30s-50s when first diagnosed. Although women account for approximately 85% of diagnoses, all patients report constant and myriad examples of gender, age, and obesity bias that affect their care.

Some rare diseases have distinctive symptoms, identified genetic mutations, and "easy" confirmatory testing; **not Cushing's**. The symptoms of high cortisol are shared by quite a few other conditions and onset is often gradual; this can make it difficult to see that everything is connected. Many patients report knowing something was wrong for years but being dismissed as "just needing to lose some weight and maybe see a therapist", and it is devastating that the **average length of time patients report knowing they were sick before receiving a diagnosis is more than six years**. Patients strongly feel that this disease is one that must become very bad before doctors will believe it. At the same time, our providers report that Cushing's Disease is the most difficult endocrine disease to diagnose.

We are encouraged by the growing number of studies that go beyond established data to introduce new concepts and deeper quality of life (QoL) understanding in the medical field. The last decade has produced several FDA approvals for drugs even with the challenge of serving a small rare patient population, and the last quarter century has seen many advancements in surgical techniques. There is a lot more to do, though. In our peer groups, we discuss these unmet needs. We form committees to identify the gaps we experience in our own care and problems that persist long after "cure". **CSR creates methods to engage membership and find our statistically significant commonalities, and then we take action.** As long as patients still struggle to make informed decisions and avoid being a passive member of their own care team when faced with so many challenges before, during, and after surgery, we consider it a mandate to work toward resolutions:

- Increase access to easy-to-understand, science-supported, comprehensive information on medical, surgical, and other types of treatment options including Traditional Chinese Medicine and neuropsychological testing
- Reduce the time it takes to identify, test, and treat any form of hypercortisolism
- Increase access to expert specialists
- Reduce the overwhelming aspects of the journey and identify opportunities for better care
- Better identify misinformation to avoid making harmful choices that sometimes contribute to a delay in diagnosis
- Increase knowledge of what to expect throughout diagnosis, treatment, recovery, and beyond
- Promote individually-focused, multiple specialty management to survive cortisol withdrawal after surgery
- Better prepare for long-term quality of life issues with more and better coping tools, referrals to appropriate specialists, removal of stigma and shame, and a reclaiming of our bodies

METHODS

Approximately 30 members of CSR joined a committee for a series of Zoom workshops in early 2022 to look at QoL issues we wish to highlight when speaking with providers and researchers. Notes from these meetings were converted into a digital survey using SurveyMonkey, then approved by the committee before being sent to CSR patient membership via e-mail (around 2000 recipients). Answers were analyzed within the survey software and converted to charts and graphs for presentation.

Data collected included demographic information (race, gender, age), disease source and current status, return-to-work behavior, autoimmune exacerbations, and 66 unique quality of life statements. 175 CSR members completed this survey.

RESULTS

We had a 9.1% (n=175) response rate in less than a week on a survey that took an average of 20 minutes to complete. This disease experience truly creates a desire to advocate for others, and once we start talking about things that are not yet in literature, we realize how intensely curious we are to know if other patients experienced things we did or come from similar backgrounds.

The majority of respondents (n=148) are from the US with the next most populous countries being Canada, Australia, and the UK. There were single patient respondents in seven other countries.

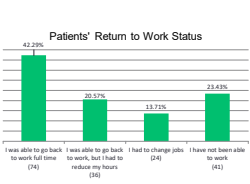
Racial breakdown of respondents: White/Caucasian 91% (n=159), Black/African American 7% (n=12), Black/Alaska Native 1% (n=2), and Asian 1% (n=2).

Many more women filled out the questionnaire than men: **women 92% (n=161) to men 8% (n=14).**

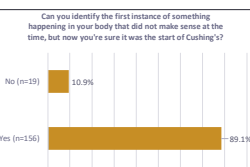
Participant age ranged from 22-88 with an average of 54 years of age.

Respondents' source and status of Cushing's: 74% pituitary (n=129), 22% adrenal (n=39), 3% ectopic (n=5), and 1% unknown (n=2). 78% have had surgery and are in remission (n=136), 11.5% are experiencing recurrence (n=20), 5% had unsuccessful surgery and remain in active Cushing's (n=9), 4% have been diagnosed but not yet had surgery (n=7), and 1.5% are still seeking diagnosis (n=3).

In the US, it is fairly standard to recommend planning for six weeks off from work for surgery and recovery. This is an unrealistically short window that many patients have no choice but to try to meet, often to their detriment.

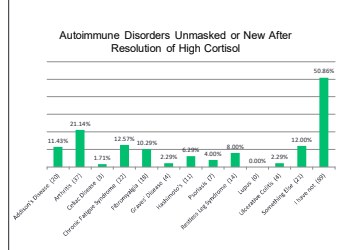


Half of respondents (n=87) had one or more dysregulated hormones during or after active Cushing's and required hormone replacement therapy, but only 22% of those confirmed that they felt adequately educated about the replacement.



Once we find out that the reason for our avalanche of symptoms and poor quality of life is persistent high cortisol, most of us can look back at photos or remember specific illnesses and realize that we had been suffering the effects of this illness for a long time.

Half of respondents listed one or more conditions they have to manage now as a result of Cushing's. Immune hits from prolonged high cortisol are well documented in literature.



- WEIGHT GAIN
- HYPERTENSION
- EXTREME FATIGUE
- PERIOD ISSUES
- ACNE
- HAIR GROWTH ON FACE
- ANXIETY
- EASY BRUISING
- FACE SHAPE CHANGE
- SKIN DISCOLORATION
- SLEEP DISTURBANCES
- MUSCLE WEAKNESS
- BONE FRACTURES
- DIABETES
- BODY PAIN
- BRAIN FOG

RESULTS (CONTINUED)

The bulk of the questionnaire consisted of 66 statements gleaned from the committee sessions, and respondents (n=175) were asked to choose "yes" or "no" if they agreed and/or that particular statement applied to them. Some examples are provided in this chart:

Statement	Yes	No
PROFESSIONAL SUPPORT		
My non-specialist doctors did not seem to understand how to accurately run blood, urine, and saliva testing for high cortisol.	58.8%	41.1%
DIEIT AND EXERCISE		
I feel extreme diet or exercise to keep the weight off while in active Cushing's.	65.7%	34.2%
PHYSICAL PRESENTATION		
People did not recognize me with Cushing's.	75.7%	24.2%
I felt like I almost had a repeat, repulsive "aura" in active Cushing's.	49.1%	50.8%
The classic Cushing's image is helpful because I saw myself in it and it was useful to help explain what was happening to me.	72.5%	27.4%
The classic Cushing's image is harmful because not everyone looks like that and it perpetuates the false narrative that we're all going to be overweight with stretch marks and a hump.	51.4%	48.5%
POST-SURGERY		
Cortisol withdrawal after a successful surgery is painful and dangerous.	71.7%	28.2%
I have been diagnosed with PTSD or OPCS as a result of my Cushing's.	6.7%	93.2%
I have not been diagnosed, but I believe I have PTSD or OPCS from Cushing's.	25.4%	74.5%
I have been diagnosed with new ASD / ADHD after Cushing's.	7.4%	92.5%
Healing is a slow process and does not only include normalization of cortisol.	96.5%	3.4%
I have recovered back to my "old normal".	29.4%	70.6%
"Old normal" is long gone and I'm still trying to determine what my "new normal" looks like.	72.0%	28.0%
HARM AND BIAS		
I was told I would be hit better and back to work about 6 weeks after surgery.	44.0%	56.0%
I experienced humiliation and/or rejection from people I knew while I was in active Cushing's.	56.5%	43.4%
I experienced fat shaming or bias in my quest for diagnosis.	58.8%	41.1%
I experienced gender bias in my quest for diagnosis.	20.5%	79.4%
PERSONAL OBSERVATIONS AND OPINIONS		
This is a disease where you must get very sick before it can be diagnosed and treated.	90.2%	9.7%
"Cure" is a dangerous word.	73.7%	26.2%
Validating the patient experience is one of the most important things my doctors can do.	96.0%	4.0%
I am frustrated by one-size-fits-all "normal ranges" of hormone levels in the blood that I do not feel are accurate to me personally.	64.0%	36.0%
I believe it is important to educate primary care providers about this condition.	99.4%	0.5%
I believe it is important to educate specialty doctors about this condition.	100.0%	0.0%
I believe it is important to educate endocrinologists about this condition.	98.2%	1.7%
I believe that the cost for blood, urine, and saliva tests, even to "rule out", is very small compared to the detrimental cost to my health from a delayed diagnosis.	95.4%	4.5%
PRE-TO-POST SURGERY		
Memory problems have led me to use adaptations such as lists and notes to myself, and I did not do this before.	73.1%	26.8%
You might need to prepare yourself to take much longer than 6 weeks, or even 6 months after surgery to return to work or normal activity.	89.1%	10.8%
CHALLENGES		
Just because my blood test results fall in normal ranges, that does not mean my symptoms are gone or that I am ok.	83.4%	16.5%
I had to fight my insurance company on one or more treatments I needed for Cushing's.	24.5%	75.4%
I believe that all the various names for high cortisol lead to misinterpretation, self-diagnosis, and confusion.	60.5%	39.4%
I feel that my health problems are all-consuming.	52.5%	47.4%
I consider myself hypervigilant for any new sign of illness or return of high cortisol.	75.4%	24.5%
I have ongoing pain.	52.0%	48.0%
I have ongoing problems with stamina.	76.0%	23.9%
I have long term memory problems.	65.1%	34.8%
I still feel so many things stressful, and it is difficult to cope.	52.5%	47.4%

CONCLUSION

The success, relative ease, and appropriateness of this type of data collection by a patient advocacy group supports plans for a future registry. Our findings inspire patients to become more proactive in their own care. Shared best practices offer new considerations for patients with similar quality of life issues. Patient-Provider communication is improved when the patient is educated and empowered with science-backed, factual data and encouraged to be their own vocal advocate. The value of an active patient advocacy group is further solidified for all stakeholders when the patients' lives improve as a direct result of their involvement with the organization.

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2022 UPDATE AND A DEEPER DIVE INTO QUALITY OF LIFE (QoL) TOPICS: A SURVEY OF 175 CUSHING'S PATIENTS, JUL 2022, CSR FUNDATION