The Alström Syndrome Journey

United States and Canada

Agenda

- Project Objectives
- Methodology
- Stages in the Alström Syndrome Journey

MAPPING THE ALSTROM SYNDROME JOURNEY

Project Objectives:

- **MAP** the diagnostic and emotional journey (including information sources) of these individuals and their caregivers
- **BRING TO LIFE** the US individuals and caregivers affected by Alström syndrome, digging into their attitudes, behaviors, wants, needs, emotional states, and the aspirations driving their decision-making
- **UNDERSTAND** the points of inflection where those affected get on and off the journey, and explore opportunities to motivate and support them
- **DIMENSIONALIZE** the words, phrases, and unique language surrounding Alström syndrome (i.e., who uses it, the meanings, symbols, and patterns of use)
- **DEFINE** moments and areas of opportunity for supporting individuals and caregivers affected by Alström syndrome in their discovery and ultimately their treatment experience

PROJECT METHODOLOGY OVERVIEW

PHASE ONE: DISCOVERY

IMMERSION

uncover the foundation

KICKOFF + ALIGNMENT

define our questions

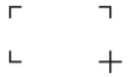
BBS + ALSTRÖM SYNDROME DIGITAL BLOGRAPHY

deep dive into the experience

IN-HOME ETHNOS

add color and perspective

PHASE TWO: DELIVERY



INSIGHTS PLAYBOOK

define the story

JOURNEY TO DIAGNOSIS MINI-DOC

bring the story to life

TOPICAL VIDEOS

dive deeper into topics of interest

BBS + ALSTRÖM SYNDROME JOURNEY MAP

follow along the way

RGDO DICTIONARY

understand the language

Alström Syndrome Journey (US/Canada)

WHO WE TALKED TO…

7 US + CAN CAREGIVERS REPRESENTING 7 DIAGNOSED INDIVIDUALS
AND 5 US + CAN INDIVIDUALS DIAGNOSED WITH ALSTRÖM SYNDROME

CAREGIVERS

Parent of nine, including 8 yr old female diagnosed with Alström syndrome

Parent of two, including 12 yr old male diagnosed with Alström syndrome

Parent of two, including 21 yr old female diagnosed with Alström syndrome

Parent of two, including 26 yr old female diagnosed with Alström syndrome

Parent of two, including 10 yrs old female - diagnosed with Alström syndrome

Parent of four, including 8 yr male diagnosed with Alström syndrome

Parent of three, including 18 yr old female diagnosed with Alström syndrome

DIAGNOSED INDIVIDUALS

27 yr old male diagnosed with Alström syndrome

36 yr old male diagnosed with Alström syndrome

27 yr old and 36 yr old males noted above are brothers

26 yr old female diagnosed with Alström syndrome

21 yr old female diagnosed with Alström syndrome

18 yr old female diagnosed with Alström syndrome

Alström syndrome, at a glance…

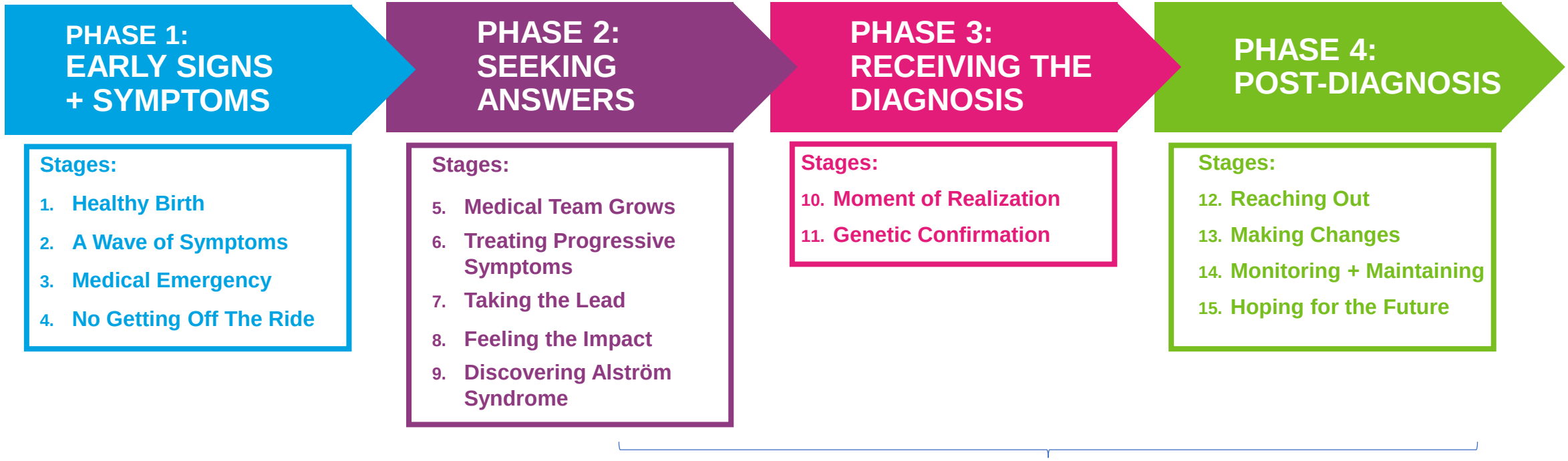
Alström syndrome is an extremely rare genetic disorder of obesity caused by a variant in the ALMS1 gene that causes serious medical problems affecting all major organ systems (including bladder, kidneys, liver, and lungs). Signs and symptoms of Alström syndrome vary among affected individuals, as does the age of symptomatic expression, progression, and severity.

SYMPTOMS OBSERVED OR MENTIONED IN THIS RESEARCH:

+ Nystagmus (wobbling eyes), photophobia (light sensitivity), and progressive vision loss specifically due to cone-rod dystrophy
+ Progressive sensorineural hearing loss and chronic ear infections
+ Heart disease, cardiomyopathy (typically within the first few years of life), and potential heart failure
+ Insatiable hunger, early, rapid weight gain/truncal obesity, difficulty losing weight
+ Kidney cysts, defects, hydronephrosis, and other renal anomalies that may progress into a need for dialysis and kidney transplantation
+ Diabetes mellitus (specifically type II diabetes)
+ Fatty liver/liver disease
+ Intellectual impairments, developmental delays (in early childhood), and/or inappropriate social behavior (potentially due to vision loss)
+ Genital and urinary tract abnormalities that impact fertility (e.g., hypogenitalism in both males and females, testicular hypogonadism in males, and in females, an underdeveloped uterus, fallopian tubes, and/or ovaries impacting menstruation)

Note: Exact progression and presentation of symptoms varies by individual

THE ALSTRÖM SYNDROME JOURNEY OVERVIEW (US + CAN)

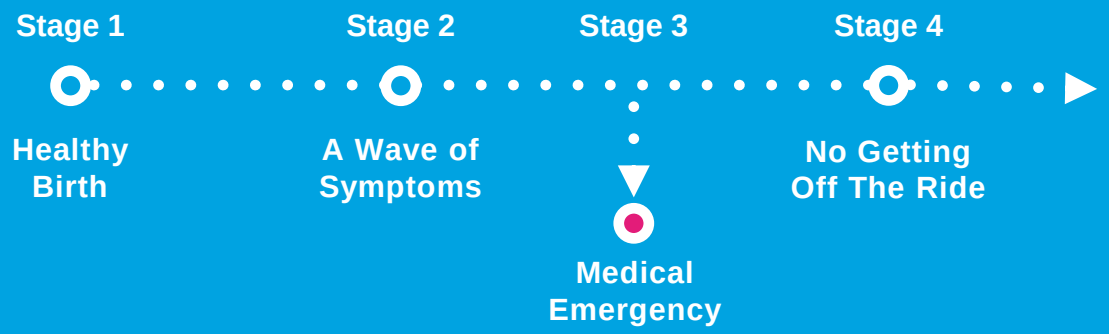


Phase 2 through Phase 4 align closely with the BBS journey.

Note that this reflects the journey of 12 individuals affected with Alström syndrome, and that there is variability in presentation and progression through the journey.

PHASE 1

EARLY SIGNS + SYMPTOMS



ALSTRÖM SYNDROME JOURNEY (US + CAN)

PHASE 1: EARLY SIGNS + SYMPTOMS (1 of 2)

1. Healthy Birth

Journeys begin with seemingly healthy babies born via normal deliveries

Even in cases of complicated pregnancies, there are typically no reasons to be concerned once the baby is delivered

Full of excitement, caregivers are free to take their children home within a few days

2. A Wave of Symptoms

Caregivers soon begin to notice a wide-range of health complications and concerns — most notably nystagmus (wobbling eyes), photophobia (light sensitivity), and insatiable hunger + rapid weight gain

The implication of eye-related symptoms and other health complications forces HCPs to take caregivers' concerns seriously

At the same time, children may present other minor health concerns, often downplayed by doctors (e.g., ear infections, dental abnormalities, or slight developmental delays)

ALSTRÖM SYNDROME JOURNEY (US + CAN)

PHASE 1: EARLY SIGNS + SYMPTOMS (2 of 2)

3. Medical Emergency (for some)

Some affected individuals' health may take a turn for the worse—experiencing heart failure due to cardiomyopathy

This critical point in the journey often means a matter of life or death

Although early warning signs may have been missed/downplayed, caregivers and HCPs sound the alarm—rushing affected individuals to specialists, the ER, and PICU

While these major medical emergencies mean affected individuals may be looked at more closely, this unfortunately does not translate to identifying Alström syndrome any faster

4. No Getting off the Ride

A constant flow of health issues keep caregivers cycling between their homes and hospitals with emotions following suit—fluctuating between a variety of feelings, worries, and concerns

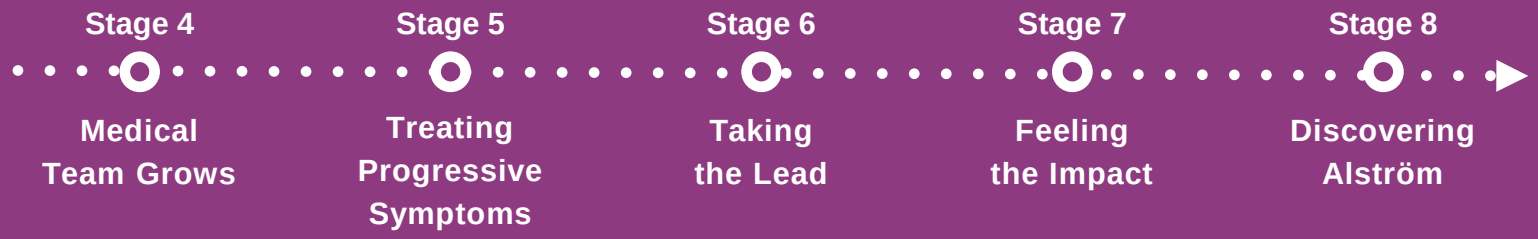
The journey gains steam as medical teams take on the challenge of uncovering what is happening with the affected individuals' health

A visual metaphor provided by a caregiver to describe her journey as a caregiver of an individual with Alström syndrome

PHASE 2

SEEKING ANSWERS

Note: At this point, the Alström syndrome and BBS journeys share many of the same stages and experiences common to searching for a rare diagnosis.



ALSTRÖM SYNDROME JOURNEY (US + CAN)

PHASE 2: SEEKING ANSWERS (1 of 2)

4. Medical Team Grows

The search for answers ramps up as HCPs recognize the need for a closer look

Caregivers + affected individuals being to see a growing list of specialists + medical professionals

The amount of appointments, tests + procedures increases as specialists dive into symptoms and conditions related to their specific areas of expertise

This stage of the journey can last from a few months to multiple years

5. Treating Progressive Symptoms

New symptoms continue to appear while others progress and intensify

Various treatment plans (medications, therapies, lifestyle adjustments) are designed to keep individual symptoms and conditions at bay

But symptomatic treatments fail to offer any long-term solutions or clarity on the individual's overall health

Note: Unlike BBS, any perceived cognitive or social impairments are typically attributed solely to vision and hearing loss

6. Taking the Lead

The responsibility of managing affected individuals' health often falls exclusively on their caregivers

This means staying on top of multiple appointments and treatment plans, while also researching as much as possible

Caregivers soon become knowledgeable experts when it comes to these complex health needs

They begin calling the shots and will leave behind any HCPs who don't take them seriously

ALSTRÖM SYNDROME JOURNEY (US + CAN)

PHASE 2: SEEKING ANSWERS (2 of 2)

7. Feeling the Impact

More than just a medical journey, the toll of seeking answers has a profound emotional impact

Families must navigate an amalgam of financial, social, and emotional challenges that effect every aspect of their daily lives

Many of these challenges never fully go away, even after a diagnosis is made

8. Discovering Alström

After months (or years) of searching and testing, affected individuals eventually present enough symptoms or conditions for someone to recognize Alström

This is usually a chance encounter (via online research, in-the-know HCPs, advocacy groups, or other caregivers + affected individuals)

ALSTRÖM SYNDROME JOURNEY (US + CAN)

SPOTLIGHT: ALSTRÖM SYMPTOMS + CONDITIONS

NOTE: *While the exact presentation and progression can vary, looking across multiple journeys offers a loose outline of the complex presentation of symptoms and conditions, as well as the lifelong impact of Alström syndrome.*

Birth:

+ Healthy birth

First Year:

+ Nystagmus (wobbling eyes) + photophobia (light-sensitivity)
+ Insatiable hunger + uncontrolled weight gain
+ Frequent ear infections + potential dental abnormalities
+ Potential Cardiomyopathy / congestive heart failure
+ Developmental delays (missed milestones)

Early Childhood:

+ Early vision loss due to cone-rod dystrophy (may use tinted glasses)
+ Early sensorineural hearing loss
+ Cognitive / behavioral delays, autism, anxiety + attention disorders
+ Ataxia (poor coordination) + mobility issues
+ Asthma + breathing complications

Puberty + Early Adulthood:

+ Progressive vision / hearing loss
+ Kidney, heart, or liver disease + complications
+ Weight-related complications (e.g., diabetes, fatty liver)
+ Thyroid complications + sex and growth hormone deficiencies

Adulthood:

+ Progressive kidney, heart, or liver disease + complications
+ Continued vision+ hearing loss / potential blindness + deafness
+ Continued struggles with insatiable hunger + uncontrolled weight gain

ALSTRÖM SYNDROME JOURNEY (US + CAN)

SPOTLIGHT: ALSTRÖM TREATMENT OPTIONS

Medications

BACTRIM® (sulfamethoxazole and trimethoprim)
For frequent ear infections

CATAPRES® (clonidine)
For attention deficit hyperactivity disorder (ADHD)

DIFLUCAN®
Anti-fungal for reducing + minimizing infections

LIPITOR® (atorvastatin)
For high cholesterol

MIDODRINE
For reducing + minimizing dizziness

MYCOPHENOLATE + TACROMILUS + VALCYTE® (valganciclovir)
For lowering risk after organ transplant

PEPCID®
Acid-reducer for gastroesophageal reflux disease (GERD)

PLAVIX® (clopidogrel)
Antiplatelet medicine to reduce the risk of heart disease

PREDNISONE
Anti-inflammatory

PROZAC® (fluoxetine)
For anxiety + panic disorders

ZOFRAN® (ondansetron)
For preventing nausea + vomiting

Procedures + Lifestyle

ORGAN TRANSPLANT
If/when affected organs cease to function properly

REDUCED CALORIE DIETS
Condition specific diets focused on monitoring calories and minimizing processed, harmful foods and additives.

Medical Devices

ASSISTIVE DEVICES
To assist with vision and hearing loss, including glasses; screen readers and text enlargers; hearing aids; cochlear implants

INHALERS
For asthma

ALSTRÖM SYNDROME JOURNEY (US + CAN)

SPOTLIGHT: THE ALSTRÖM MEDICAL TEAM

PEDIATRICIANS

Receive initial concerns, track along with overall health, and refer to relevant specialists.

CARDIOLOGISTS

Monitor and assess the heart, including the response to, and treatment of cardiomyopathy in some individuals.

ENTs

Assess, monitor, and treat breathing and hearing complications, including frequent ear infections, and progressive hearing-loss.

OPTOMETRISTS

Diagnose nystagmus and light-sensitivity, cataracts, and astigmatism, conduct vision tests, prescribe glasses, monitor progressive vision loss, and refer to ophthalmologists or other specialists, when necessary.

OPHTHMALOGISTS

Conduct ERGs, MRIs; diagnose cone-rod dystrophy.

NEUROLOGISTS

Explore and monitor the presence of any developmental delays, cognitive delays, or autism.

DIETICIANS

Offer recommendations and dietary support, helping perfect daily meal schedules and routines.

ENDOCRINOLOGISTS

Monitor hormone production, keeping a close eye on issues related to metabolism (notably, diabetes), the thyroid and adrenal glands.

NEPHROLOGISTS

Monitor, assess, and manage complications with kidney-function, including kidney disease and decreased function.

HEPATOLOGISTS

Track and monitor liver function, including complications from weight gain and obesity, notably non-alcoholic steatohepatitis (i.e., fatty liver disease)

GENETICISTS

Eventually brought on to test for any genetic variants causing/contributing to symptoms and overarching conditions pre-diagnosis.

THERAPISTS

Various types (e.g., PT, OT, ABA, speech, vision) brought on to increase and improve daily functions and overall quality of life.

ALSTRÖM SYNDROME JOURNEY (US + CAN)

SPOTLIGHT: CHALLENGES WITH HCPs

NARROW FOCUS

Doctors “don’t know what they don’t know,” and while caregivers do not fault them, many note that it can be frustrating when it seems doctors are unable or unwilling to look beyond their specialties or the most obvious answers.

POOR COMMUNICATION

Caregivers believe that the best care comes when HCPs are willing to communicate and work together, which is why many appreciate the attention they receive at research clinics.

REFUSING TO RESEARCH

One of the biggest pain points comes when doctors are not willing to learn about the individual’s complicated medical history and needs. This forces caregivers to constantly educate (and reeducate) doctors on things they should already know.

“GIVING UP”

During the journey, caregivers can be confronted with dead-ends or doctors who “give up.” The dismissive nature with which some HCPs share their learnings (or lack thereof) can leave caregivers feeling hopeless and angry.

PHASE 3

GETTING THE DIAGNOSIS

Note: At this point, the Alström syndrome and BBS journeys share many of the same stages and experiences common to receiving a rare diagnosis.

ALSTRÖM SYNDROME JOURNEY (US + CAN)

PHASE 3: GETTING THE DIAGNOSIS

9. Moment of Realization

List of symptoms + conditions, and photographs of diagnosed individuals bring certainty that Alström syndrome is in fact what they've been looking for

With this certainty comes a slew of emotions caregivers must grapple with as their long search for answers begins to come to an end

Caregivers and HCPs arrive at a clinical diagnosis "checking off the boxes" symptoms + conditions

While having a name "on paper" offers some relief and loose guidelines, a clinical diagnosis does little to change caregivers' approach to treatment

10. Genetic Confirmation

Although many may have received genetic testing during their initial searches for answers, these tests routinely come with inconclusive results

But after discovering Alström syndrome, caregivers seek genetic testing to provide concrete confirmation

In some cases, advocacy groups (namely, Alström syndrome International (ASI) and the late Jan Marshall) may step in to facilitate genetic testing and confirm a diagnosis

Although these tests remove any lingering doubt, it is considered by many to be a "nice-to-have," rather than a critical stage in the diagnostic journey

ALSTRÖM SYNDROME JOURNEY (US + CAN)

SPOTLIGHT: RECOGNIZING ALSTRÖM IN A 2nd CHILD

"It was more just like, okay we know we had gone through all this stuff with my older brother who was diagnosed and then 8 years later here comes me and I seem fairly normal, but then they noticed the nystagmus in my eyes. Of course my mom was like 'Oh god not again!' So my diagnosis was fairly straight forward, just because they already had my older brother's diagnosis. So for my progression [of symptoms], in a sense I was ready for it because my brother had gone through the same thing."

- 27 yr old male diagnosed with Alström syndrome)

Notes from ASI Conference:

Though the caregivers in this research all had one affected child, Rhythm attendees to the Alström Syndrome International conference met many families with multiple affected children. For example, one family had twin girls; another retired couple had two adult children (one had passed away), and grandparents talked about having 3 of 3 grandchildren (same parents) with Alström syndrome.

PHASE 4

POST – DIAGNOSIS

Note: At this point, the Alström syndrome and BBS journeys share many of the same stages and experiences common to living with a rare diagnosis.

ALSTRÖM SYNDROME JOURNEY (US + CAN)

PHASE 4: POST-DIAGNOSIS (1 of 2)

11. Reaching Out

Having felt alone and socially isolated throughout their search for answers, many seek out other families and patient advocacy groups

They look to share best practices regarding treatment, discuss what to expect, and support each other as the only people who truly “get it”

Others, however, may prefer to distance themselves from the community — wishing to avoid the realities of the future, or simply finding it easier to cope by disassociating with Alström syndrome

Recognizing the impact of Jan Marshall (ASI). ***Click image for video*** *– via Greater Baltimore Medical Center*

12. Making Changes

Caregivers shift from “what is this” to “what do we do” — taking a “when” not “if” approach to progressive symptoms and conditions

Resources + support from HCPs, community members, schools, and other outlets guide them as they create an environment where their children can grow healthy + independent

Mindful of potential future health complications, caregivers work to better understand nutrition and implement healthier dietary lifestyles

ALSTRÖM SYNDROME JOURNEY (US + CAN)

PHASE 4: POST-DIAGNOSIS(2 of 2)

13. Monitoring + Maintaining

With no blueprint of how to best approach Alström syndrome, caregivers take steps to continuously monitor and stay on top of their children's health

This means regular check-ins with members of the care team to keep an eye on progressive symptoms and conditions

While there is no exact timeline, caregivers take these steps to ensure their entire family is prepared for the future

14. Hoping for the Future

Many caregivers' initial instincts are to shelter their children, but realize that growth requires trial and error

With routines firmly in place and the affected individuals' health stable, families look forward with tempered expectations for the future

Their focuses shift away from simply managing, as caregivers + affected individuals strive to foster independence

Increased awareness and advances in treatment options provide these families with hope that the future will only continue to improve the Alström syndrome experience

ALSTRÖM SYNDROME JOURNEY (US + CAN)

SPOTLIGHT: FUTURE TREATMENT OPTIONS

"It's not just her quality of life that would be affected if she would no longer be controlled by hunger. Every single thing would not revolve around food for her or the family too. That's a battle that we have to always be aware of.

I can't even imagine her not constantly being consumed by the thought of food. It'd be a different her, and in a good way because she'd be able to focus more on things that kids her age focus on… instead of, 'When is my next meal? Is it time for a snack?'

Even our family friends that were sitting in the conference hearing [the Rhythm] presentation were almost in tears thinking about how different it would be for her, and they're not even in our family. It would be an entirely different reality for everyone in her life."

- Mother of 2, 1 child diagnosed with Alström syndrome)

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