The Alström Syndrome Journey

United States and Canada
Agenda

• Project Objectives
• Methodology
• Stages in the Alström 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.
PHASE ONE: DISCOVERY

- IMMERSION: uncover the foundation
- KICKOFF + ALIGNMENT: define our questions
- BBS + ALSTROM SYNDROME DIGITAL BLOGGRAPHY: 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 + ALSTROM 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

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
- 27 yr old male and 36 yr old male noted above are brothers
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/trunkal 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
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.
EARLY SIGNS + SYMPTOMS

Stage 1
Healthy Birth

Stage 2
A Wave of Symptoms

Stage 3
Medical Emergency

Stage 4
No Getting Off The Ride
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).
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.
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.
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
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 affect 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).
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
### Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>BACTRIM</strong> (sulfamethoxazole and trimethoprim)</td>
<td>For frequent ear infections</td>
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<tr>
<td><strong>CATAPRES</strong> (clonidine)</td>
<td>For attention deficit hyperactivity disorder (ADHD)</td>
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<tr>
<td><strong>DIFLUCAN</strong></td>
<td>Anti-fungal for reducing + minimizing infections</td>
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<td><strong>PEPCID</strong></td>
<td>Acid-reducer for gastroesophageal reflux disease (GERD)</td>
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<tr>
<td><strong>MYCOPHENOLATE + TACROMILUS + VALCYTE</strong> (valganciclovir)</td>
<td>For lowering risk after organ transplant</td>
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<tr>
<td><strong>LIPITOR</strong> (atorvastatin)</td>
<td>For high cholesterol</td>
</tr>
<tr>
<td><strong>MIDODRINE</strong></td>
<td>For reducing + minimizing dizziness</td>
</tr>
<tr>
<td><strong>PROZAC</strong> (fluoxetine)</td>
<td>For anxiety + panic disorders</td>
</tr>
<tr>
<td><strong>MYCOPHENOLATE + TACROMILUS + VALCYTE</strong> (valganciclovir)</td>
<td>For lowering risk after organ transplant</td>
</tr>
<tr>
<td><strong>PLAVIX</strong> (clopidogrel)</td>
<td>Antiplatelet medicine to reduce the risk of heart disease</td>
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<tr>
<td><strong>PREDNISONE</strong></td>
<td>Anti-inflammatory</td>
</tr>
<tr>
<td><strong>PROZAC</strong> (fluoxetine)</td>
<td>For anxiety + panic disorders</td>
</tr>
<tr>
<td><strong>ZOFRAN</strong> (ondansetron)</td>
<td>For preventing nausea + vomiting</td>
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### Procedures + Lifestyle

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<tr>
<th>Procedure</th>
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<tbody>
<tr>
<td><strong>ORGAN TRANSPLANT</strong></td>
<td>If/when affected organs cease to function properly</td>
</tr>
<tr>
<td><strong>REDUCED CALORIE DIETS</strong></td>
<td>Condition specific diets focused on monitoring calories and minimizing processed, harmful foods and additives.</td>
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### Medical Devices

<table>
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<tbody>
<tr>
<td><strong>ASSISTIVE DEVICES</strong></td>
<td>To assist with vision and hearing loss, including glasses; screen readers and text enlargers; hearing aids; cochlear implants</td>
</tr>
<tr>
<td><strong>INHALERS</strong></td>
<td>For asthma</td>
</tr>
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### ALSTRÖM SYNDROME JOURNEY (US + CAN)

#### SPOTLIGHT: THE ALSTRÖM MEDICAL TEAM

<table>
<thead>
<tr>
<th>Medical Team</th>
<th>Responsibilities</th>
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<tbody>
<tr>
<td><strong>PEDIATRICIANS</strong></td>
<td>Receive initial concerns, track along with overall health, and refer to relevant specialists.</td>
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<tr>
<td><strong>CARDIOLOGISTS</strong></td>
<td>Monitor and assess the heart, including the response to, and treatment of cardiomyopathy in some individuals.</td>
</tr>
<tr>
<td><strong>ENTS</strong></td>
<td>Assess, monitor, and treat breathing and hearing complications, including frequent ear infections, and progressive hearing-loss.</td>
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<tr>
<td><strong>OPTOMETRISTS</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>NEPHROLOGISTS</strong></td>
<td>Monitor, assess, and manage complications with kidney function, including kidney disease and decreased function.</td>
</tr>
<tr>
<td><strong>HEPATOLOGISTS</strong></td>
<td>Track and monitor liver function, including complications from weight gain and obesity, notably non-alcoholic steatohepatitis (i.e., fatty liver disease).</td>
</tr>
<tr>
<td><strong>GENETICISTS</strong></td>
<td>Eventually brought on to test for any genetic variants causing/contributing to symptoms and overarching conditions pre-diagnosis.</td>
</tr>
<tr>
<td><strong>THERAPISTS</strong></td>
<td>Various types (e.g., PT, OT, ABA, speech, vision) brought on to increase and improve daily functions and overall quality of life.</td>
</tr>
<tr>
<td><strong>DIETICIANS</strong></td>
<td>Offer recommendations and dietary support, helping perfect daily meal schedules and routines.</td>
</tr>
<tr>
<td><strong>ENDOCRINOLOGISTS</strong></td>
<td>Monitor hormone production, keeping a close eye on issues related to metabolism (notably diabetes), the thyroid and adrenal glands.</td>
</tr>
<tr>
<td><strong>NEUROLOGISTS</strong></td>
<td>Explore and monitor the presence of any developmental delays, cognitive delays, or autism.</td>
</tr>
<tr>
<td><strong>OPHTHALMOLOGISTS</strong></td>
<td>Conduct ERGs, MRIs; diagnose cone-rod dystrophy.</td>
</tr>
<tr>
<td><strong>NARROW FOCUS</strong></td>
<td><strong>POOR COMMUNICATION</strong></td>
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<tr>
<td>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.</td>
<td>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.</td>
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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.
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.
“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 straightforward, 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.
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.

Stage 11  Stage 12  Stage 13  Stage 14
Reaching Out  Making Changes  Monitoring + Maintaining  Hoping for the Future
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.

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.

Recognizing the impact of Jan Marshall (ASI). Click image for video – via Greater Baltimore Medical Center.
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 and 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.
“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)
This research was done by Rhythm Pharmaceuticals and Now What. Thank you to Alström Syndrome International, and all the participants for their contributions.