Alström Syndrome UK
Strength for today, hope for the future

Alstrom Syndrome Journey to Diagnosis Report

Contents

Introduction

Alstrom Syndrome UK

Alström Syndrome UK (ASUK) was established in 1998 and is a registered charity providing information and support to individuals and families affected by Alström Syndrome (AS) and to the service providers working with them. ASUK works in partnership with Birmingham Women's and Children's Hospital and the Queen Elizabeth Hospital Birmingham to deliver a highly specialised service, funded by NHS England. As a patient led organisation, the needs and wishes of people living with AS remain at the heart of everything we do. We aim to; provide information and personalised support, raise awareness, promote pioneering research and enable better treatments and monitoring through the AS multi-disciplinary clinics.

Alstrom Syndrome

Alström Syndrome (AS) is a recessively inherited genetic condition which is ultra-rare and extremely complex. Symptoms include retinal dystrophy, nystagmus, photophobia, hearing loss, obesity, insulin resistance, diabetes, cardiomyopathy and can affect the liver and kidneys and result in other associated complications. The condition is progressive, but it is important to note that not all the complications associated with AS occur in everyone affected. Symptoms can also present at different stages making diagnosis difficult. Prevalence is thought to be around 1 in a million and there are currently 88 people diagnosed with AS in the UK (March 2023). A medical handbook and consensus clinical management guidelines for AS can be found on the ASUK website.

Breaking Down Barriers

ASUK co-founded Breaking Down Barriers in partnership with The Sylvia Adams Charitable Trust. Breaking Down Barriers is a network of over 70 organisations providing support to people affected by rare and genetic conditions. We work together to learn, develop, and share good practice. Promoting equity, diversity and inclusion (EDI) is at the centre of what we do. Our Experts by Experience Advisory Group help us to understand the lived experiences of people from diverse and marginalised communities who are affected by rare and genetic conditions. We create safe spaces for learning and collaboration, deliver training and run a community outreach project. We unite and strive for equitable access to services and support for all.

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Foreword

As an organisation we work with, and on behalf of people living with Alström Syndrome (AS). We understand the devastating and life-threatening consequences of a delayed diagnosis and the impact this can have on individuals, parents, carers and wider family members.

Approximately 40% of babies with AS experience heart failure between the age of 3 weeks and 4 months[1]. It is difficult to give a more accurate figure as there are cases where tragically babies die without an AS diagnosis being confirmed. Parents often describe the agony of having a child in heart failure and being told they may not survive. Where babies do survive, their parents then go on to witness their child gaining excessive weight and their eyesight deteriorating with no explanation as to why this is happening to their child.

The impact of receiving a diagnosis of AS should never be underestimated. Parents often describe the feelings of grief, fear, guilt, blame and shame that they experienced when given a diagnosis that completely changes their lives.

Receiving an accurate and timely diagnosis with access to support, expertise and accessible information is crucial. While speed is important, so is the essential support that people need at the point of diagnosis and beyond.

Thankfully, we are starting to see the average age of diagnosis dramatically reducing. In 2022/23, our data shows the average age of diagnosis for new referrals was 7 years compared to 20 years in 2018/19. This is a major step forward but still much more needs to be done.

We have identified a number of key observations and recommendations within this report that have been supported by clinicians within the AS highly specialised service. We will continue to work with people with lived experience, clinicians, researchers, commissioners, policy makers and other charity representatives to advocate for further developments to improve the experiences, health outcomes and quality of life for people living with AS.

It is encouraging to see the importance of an early diagnosis for people living with rare conditions being prioritised in the UK and the initiatives that are being developed in partnership with the rare disease community. In recent years, there has been advancements in genomics including the introduction of the Genomic Medicine Service and the National Genomic Test Directory. These developments aim to provide a faster diagnosis and a more equitable service. We are involved in initiatives such as the UK Rare Diseases Framework and we are pleased that one of the 4 main priorities is ‘helping patients get a final diagnosis faster’. We are also involved in various genomic research projects including the Generation Study, led by Genomics England to explore the benefits, challenges and practicalities of sequencing over 100,000 newborn babies to identify genetic conditions.

While we welcome these developments, our findings, and the evidence we have gathered in this report suggests that more needs to be done to improve the experiences of people receiving a

diagnosis of AS. While technology appears to be advancing at pace, unfortunately the support services, systems and pathways are just not keeping up.

I would like to thank everyone within the AS community who took part in this Journey to Diagnosis report and to those who continually and generously share their lived experience to influence change and benefit others.

We are stronger together and we have hope for the future.

Kerry Leeson-Beevers
Alstrom Syndrome UK/Breaking Down Barriers Chief Executive

Executive Summary

ASUK commissioned this report to gain a better understanding of the journey to diagnosis and identify recommendations to improve patient and family experiences and health outcomes.

Let's set the scene, the joy of having your first born turns to despair as you know something just isn't quite right. They have an un-controllable hunger, they are gaining weight at a rapid rate and the wobbly eyes and shying away from the light, which you thought was normal for a newborn may mean they will lose their sight. Getting passed from pillar to post with no real answers leaves you anxious for what the future holds. As you wait for years with no answers your child's health continues to deteriorate with no solutions or treatments to help or support you.

What could an early diagnosis mean for this family?

An early diagnosis could lead to appropriate treatment and management of their child's symptoms, as well as personalised support and improved outcomes for the whole family.

This story is common amongst families living with AS and this is why a quicker diagnosis with the right support, is what we should all be striving for.

Despite the identification of the ALMS1 gene, the advancements in genomic technology and the availability of genetic testing throughout the UK, developments still need to be made to improve the diagnostic odyssey. People with AS often face a difficult and unpredictable journey to diagnosis, moving from clinician to clinician, seeking the much-needed specialist advice from those who understand the nature of the condition best. Although AS, has a unique set of features it is difficult for clinicians to instantly recognise.

There are a few rare conditions that have similar characteristics to AS and have early onset symptoms such as nystagmus, photophobia, obesity, and cardiomyopathy. Awareness of AS amongst clinicians is limited and symptoms are often dealt with independently of one another.

The age of onset of certain AS symptoms can vary from patient to patient which can further complicate the path to diagnosis. It is also unreasonable to expect every clinician to know about and recognise every one of the over 8,000 rare conditions.

Summary of Key Findings

1. **Timeline to diagnosis**
   Patients and their families are waiting a significant amount of time for an accurate diagnosis. The Covid-19 pandemic further exacerbated this, leading to further delays and missed diagnostic opportunities.
2. **Route to diagnosis**
   Depending on which symptoms present first in a patient affects the clinical pathway, the clinical decisions that are made, and ultimately the speed and effectiveness at which a patient is diagnosed.
3. **Accessing a correct diagnosis**
   Some patients receive an incorrect diagnosis before being finally diagnosed with AS and are frequently subject to multiple incorrect referrals.
4. **Health Equity**
   Patient outcomes vary depending on various factors, such as where a patient lives, their religious and cultural beliefs, their background, education and awareness of rare disease and related conditions.
5. **Information and Awareness**
   Patients and their families have told us they believe that most medical professionals have limited or no knowledge or understanding of AS. We also learned of cases where a families' independent research via the internet and support from patient organisations like ASUK has been the key factor in getting the right diagnosis.

Summary of Key Recommendations

(Full recommendations & further information about implementation can be found on pages 18-21)

1. **Targeted and widespread training and awareness**
   Encouraging healthcare providers to 'Think Rare' and highlighting the clinical features of AS.
2. **Highlighting the first 3 key symptoms of AS**
   Through training, awareness raising and updating the AS clinical guidelines - linking with weight management clinics, cardiac and ophthalmology services and promoting genetic testing.
3. **Development of clinical and diagnostic pathways**
   Including when and how to refer for genetic testing and signposting to ASUK and the highly

specialised service.

4. **Development of genetic support services**

   No one should be left with a diagnosis they don't understand – promoting the need for rapid support and appropriate signposting.

5. **Involving people with lived experience**

   Including diverse voices and experiences in the development of services and provision of resources.

6. **Encouraging organisations to join the BDB network**

   To learn and understand the importance of addressing Equity, Diversity and Inclusion and how this can impact health outcomes and access to services.

The report highlights gaps in knowledge and areas requiring further development to enable patients and their families to receive a timely diagnosis and the support they need.

We understand the limitations of this research study. The report is patient centred, concentrating on people's lived experiences and information, which is a crucial place to start. Our next step is to gather wider perspectives, including healthcare professionals to look in more detail at healthcare data and gather their feedback and experiences to see if and how our findings and recommendations can be implemented to see real change.

We also plan to carry out a consultation exercise with the 70 + rare condition organisations that we work with as part of the BDB Network. We will support them to consult with their communities and gather evidence that will allow us to understand the journey to diagnosis within the wider rare disease community.

This report is not the end - these findings will provide a basis for future developments in the hope that we can support a faster and more supportive diagnosis, not only for people impacted by AS, but potentially for others living with rare conditions.

Research Method

ASUK conducted research into a sample of patients from the ASUK database. These patients were diagnosed between 1st April 2020 – 1st December 2022 and vary in age, ethnicity and are based in different locations around the UK. The research involved a combination of interviews with families, an analysis of demographic data from the ASUK database and hospital, social care, and education reviews. ASUK used a patient-centred approach to explore patient experiences. Questions focused on the patient's journey and covered multiple aspects of AS, such as journey to diagnosis, coordination of care, awareness and access to treatment, services, information, and support.

Research Sample

17 people were diagnosed during this time, and they are representative of the diversity of patients diagnosed on the ASUK database, particularly in terms of ethnicity as indicated in the Patient Ethnicity diagram (pictured right).

The current age of patients in our research sample ranges from 7 months to 20 years and the map below shows the geographical spread.

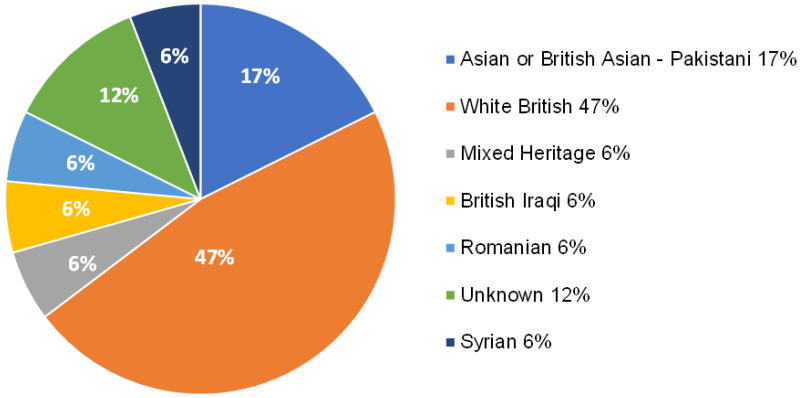
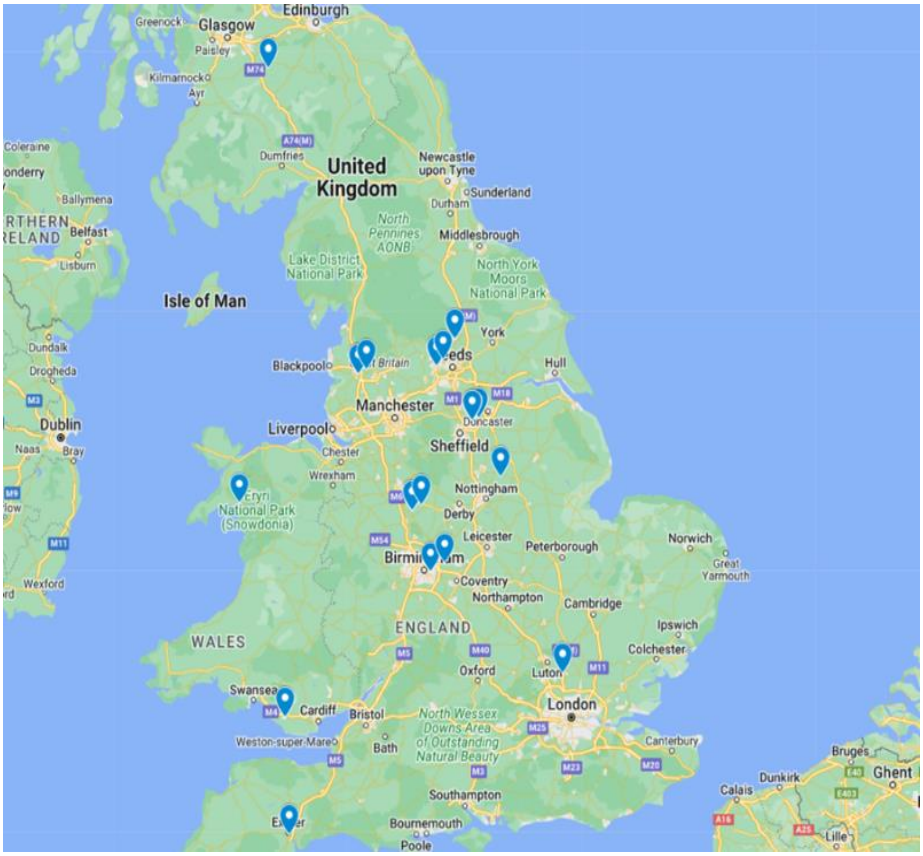


Figure 1 - Patient Ethnicity



Geographical Location

Objective

To better understand the Journey to Diagnosis for people diagnosed with AS.

We wanted to learn more about:

- When symptoms first appear and how they are managed.
- Symptoms or conditions that lead to referrals.
- Symptoms or referrals that lead to diagnoses.
- Gaps in knowledge and understanding the reasons why.
- Quality and co-ordination of care.
- Access to information and support.
- Management, treatment options and timelines.
- When ASUK and/or other support services are first utilised.

Outcomes

We plan to use these research findings to enable us to:

- **Promote a faster and more effective diagnosis**
- **Targeted awareness campaigns**
- **Raise awareness about key symptoms of the condition**
- **Promote early genetic testing and identification of key 'red flag' symptoms, for example, the combination of a visual impairment and obesity**
- **Improve the patient experience and long-term health outcomes**

Diagnosis

A prompt diagnosis and use of appropriate health and care pathways is imperative to a good quality of life and access to effective support and treatment for AS patients. In the absence of a diagnosis or correct diagnosis, it is difficult for patients and their families to manage their condition appropriately. A delay in diagnosis or misdiagnosis often means being subject to multiple tests, having to attend many avoidable medical appointments and subsequently receiving incorrect treatments. This can lead to significant distress for the patient and their families. Our research has highlighted some of the huge barriers' families have experienced in reaching an accurate diagnosis. This not only has a detrimental effect on patients and families but also results in inefficient use of an already overwhelmed NHS service.

Timelines to diagnosis

Our research has indicated severe delays in patients getting a timely diagnosis. From the graph (right) you will notice that 41% of patients had to wait between 5-20 years for a diagnosis. This delay risks further health deterioration, complications and not receiving the targeted treatments and support from the AS highly specialised multi-disciplinary clinics.

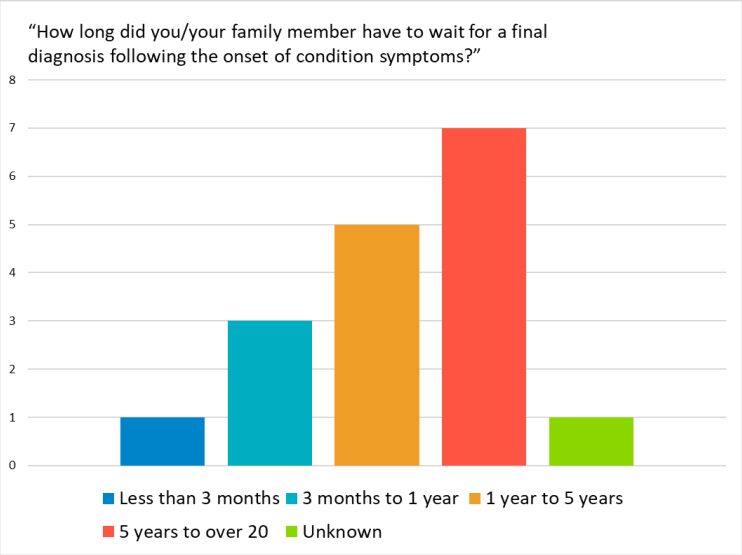


Figure 2 – Time to diagnosis

Route to diagnosis

Understanding the patient pathway is key to establishing the key factors related to a successful, early AS diagnosis versus a delayed and problematic one. We examined the routes that patients followed (Figure 3, below) and the symptoms that initially presented (Figure 4) that directly led to an AS diagnosis.

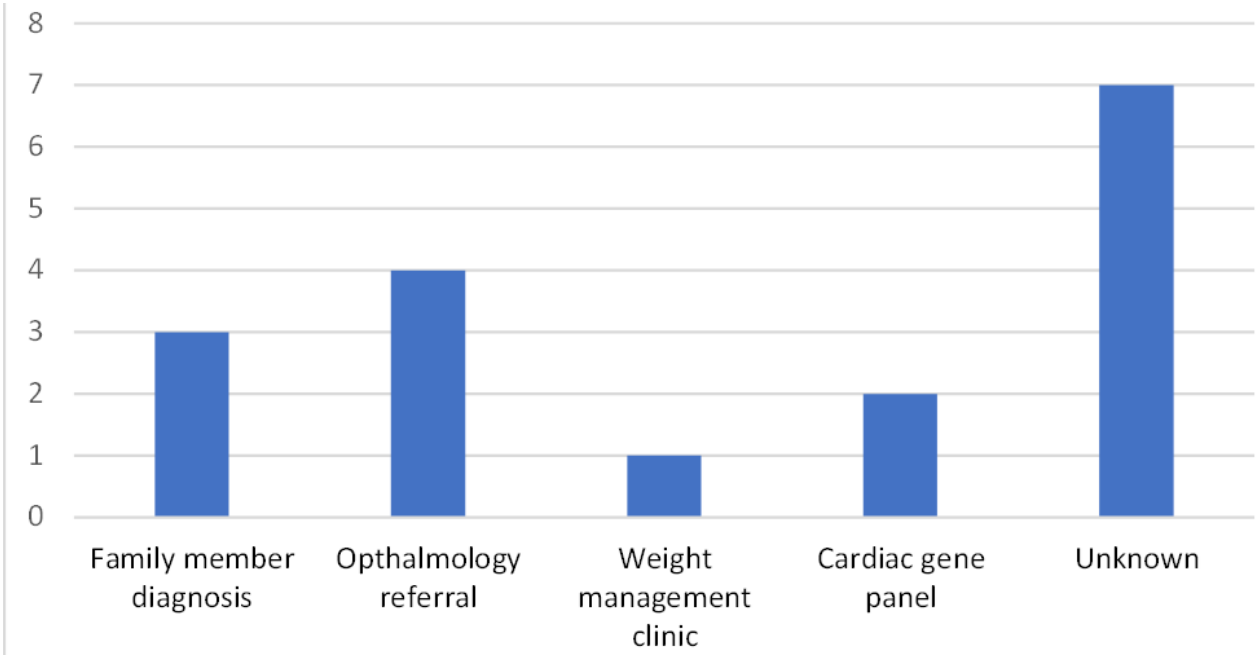


Figure 3 – Route to diagnosis

AS Symptoms and Diagnosis

All families interviewed reported a difficult diagnostic process from the onset of symptoms until they obtained a definitive diagnosis. The length of time between the onset of symptoms and diagnosis varies (Figure 2) and appears to be dependent on the type and severity of symptoms.

The top 3 initial symptoms presented by patients were **obesity, cardiovascular disease**, **and visual impairment.** Patients who presented with cardiomyopathy and visual impairment in infancy or early childhood received a quicker diagnosis compared to patients with an absence of, or later onset of these symptoms.

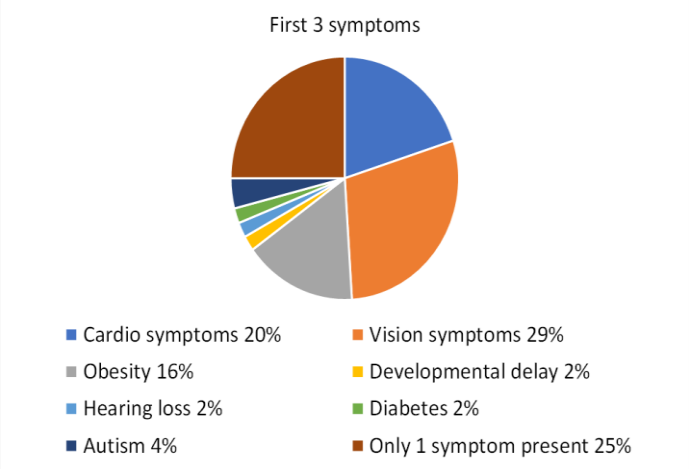


Figure 4 – First 3 AS symptoms

Cardiovascular disease

The route to diagnosis for 12% of patients in the study was via a cardiac gene panel following onset of cardiovascular symptoms in early life (<1 year).

For one of these patients, a clinical decision was made not to proceed with a cardiac transplant, and she sadly passed away at 4 months old. At this stage, it is unclear whether an early AS diagnosis impacts the decision-making process as to the suitability of patients for a transplant.

"We were told that the transplant list was too long and that my daughter wouldn't have any quality of life with a diagnosis of Alström Syndrome anyway."

Father of AS patient (14), November 2022

In the UK, heart transplants have been successful in three children with AS (including patient 7 in this study). Sadly, we have not had any successful heart transplants in adult patients. Although further information is needed to examine all the facts, the quote above illustrates how parents believe that the decision not to put their child on the transplant list was a direct result of the clinician believing that their child would have no quality of life with a diagnosis of AS.
This needs further investigation to decipher what impacts the decision-making process and how the final decision is ultimately made.

Additional findings

- Dilated cardiomyopathy is one of the most common, first AS symptoms to present - 58% of the patients studied presented with cardiovascular disease as 1 of the 3 first symptoms of AS (Figure 4).
- Onset of cardiomyopathy can vary between infancy, later childhood and adulthood.
- Patients with early onset of symptoms are diagnosed with AS more quickly than those without.

Obesity

Obesity is a relatively consistent and important early symptom of AS, with more than half of those studied presenting with rapid weight gain in their first year (53%).

One of ASUK's most recent referrals (patient 17 in this study) was identified through a Paediatric Weight Management Clinic. This clinic is one of 15 currently working with obese patients across England. These clinics, and those offering similar services to support people affected by obesity, could significantly contribute to the identification of patients with AS. In addition, this patient came to the UK in 2017 as a refugee but the AS diagnosis was not confirmed until 2022. When ASUK visited the family at home with an interpreter, parents confirmed that the child also had an older sibling with the same condition. A further visit by ASUK to the child's school also revealed another possible family member with the same condition.

ASUK are now working to support the family to access the specialist clinics and providing information and support to health and education professionals.

"Obesity, visual impairment and autism were the only 3 symptoms presenting (in my son) up to the age of 5 and his heart was fine - the result of this meant he was nearly 5 years old before we received a diagnosis".

Father of AS patient (9), August 2022

Visual Impairment

More than half of the patients in this study presented with cone-rod dystrophy before the age of 1 resulting in photophobia and nystagmus. Visual impairment was also 1 of the 3 initial symptoms presenting in 88% of patients included (Figure 4).

Additional Findings

- Patients with visual impairment and no other obvious symptoms waited longer for an AS diagnosis.
- Patients with visual impairment and cardiomyopathy were diagnosed much more quickly, either in infancy or early childhood.
- 47% of patients were diagnosed with photophobia before the age of 1.
- 41% of patients were diagnosed with nystagmus before the age of 1.

Accessing a correct diagnosis

Patients with AS and their families can face significant delays in accessing a correct diagnosis. 2 of the 17 patients in the study received a diagnosis of Bardet Biedl Syndrome and Leber Congenital Amaurosis before they were able to access further genetic tests and receive an accurate diagnosis of AS. These findings are concerning. If patients do not receive a timely diagnosis, this leads to a delay in them being able to access effective treatment and monitoring and can impact on their quality of life.

Our research highlighted that patients and families attend numerous GP and hospital appointments before their AS diagnosis is confirmed. The family of patient 4 told us that their child's early life was fraught with multiple appointments to the GP, community paediatrician and hospital clinicians. They had concerns about her eyesight, feeding difficulties and failure to meet expected milestones for crawling, walking and speech. Unfortunately, due to inconsistencies in terms of the medical professionals they saw and a lack of awareness and knowledge, this patient was not reviewed and assessed holistically. It wasn't until mum pushed for a referral to Alder-Hey Hospital that progress started to be made. This family live in a remote part of the UK, 2 hours from the hospital where they eventually received a diagnosis.

Covid-19 Pandemic

Over 50% of families we spoke to feel the Covid-19 pandemic caused a delay in their access to treatments, support, and diagnosis. Even after the lockdown, face to face appointments and consultations were cancelled. This led to feelings of worry, anxiety, and isolation. There were missed opportunities for children and young people to be examined in person and for parents to speak directly with professionals to share and explore their worries and concerns.

We also learned of some of the positive outcomes resulting from the pandemic; the use of technology was accelerated which gave patients with AS the opportunity to attend Telemedicine Clinics. Some families we spoke to said that this was a huge benefit to them as travel times to clinics are often long and difficult due to issues relating to mobility and vision.

Genetic Tests

Genetic testing in the UK has propelled forward in the last few years, with more people gaining a quicker diagnosis. Sadly, support services appear to be falling short in terms of access to support, information and signposting when a diagnosis is given to a patient and their family.

Genetic testing has given 18% of our research participants a diagnosis before the age of 1, this is hugely beneficial as it helps to put an end to some of the uncertainty and allows targeted treatment and support to be received immediately.

Timely psychological support and genetic counselling alongside a 'rapid' diagnosis is vital to minimise distress and maximise the benefits to patients and their families. The nature of any genetic condition can cause a range of emotions. Families tell us, specialists such as genetic counsellors, family support workers, and psychologists, as well as members of support groups like ASUK, can be extremely helpful.

While the mainstreaming of genetics may lead to a faster diagnosis, the experiences of diagnosis for patients and families may not be so positive. Access to appropriate information, support and signposting and establishing a care pathway is essential.

One of the families we spoke to shares their experience of genetic testing. Their local Ophthalmologist organised genetic testing. A letter was later sent by post to the family informing them of the results of the genetic test. The letter confirmed a diagnosis of AS but used complex medical and scientific terminology and lacked any information about the condition, its symptoms, and the treatments available. It also failed to signpost to the highly specialised service or any support services.

Parents were left to search the internet to try and find further information which led them to contact ASUK. ASUK were able to talk through the condition with parents and give them clear information about how to request a referral to the multidisciplinary clinics.

In this instance, ASUK liaised between the family, local healthcare professionals and the specialist team to put interim measures in place to monitor the patient until they could be seen by the specialist team.

The whole process of receiving a diagnosis in this way, caused the family significant distress and highlights how critical appropriate signposting, support, information and a clear care pathway is at the point of diagnosis.

"My daughter's early years were fraught with worry, trying to navigate a complicated healthcare system, trying to find appropriate help and support was extremely difficult. There was no consistency in terms of staff at our local hospital, on each visit we would be assessed by a different locum, most of whom lacked any knowledge, awareness, or expertise."

Mother of AS patient (4) interviewed, August 2022

Information and Awareness

Many of the families we spoke to shared concerns about the lack of AS awareness amongst healthcare professionals. We also heard of parent's frustration with GPs for not referring their child to the appropriate specialist and in some cases not referring to anyone at all. Parents did however acknowledge that it is impossible for every healthcare professional to know about every rare condition. However, training on what to do when presented with multiple or unusual symptoms and the availability of sources of information about rare conditions and referrals could potentially support healthcare professionals in the diagnostic process.

The results from all our patient interviews highlighted the importance of healthcare professionals having an awareness and understanding of Alström Syndrome.

The effects are profound and can include:

- Delayed recognition of symptoms.
- Misdiagnosis or underdiagnosis: Some of our patients received an incorrect diagnosis or were labelled with other more common conditions that share similar symptoms. This resulted in a delay in receiving appropriate care and management.
- Prolonged diagnostic journey.
- Limited access to genetic testing.
- Psychosocial impact: patients who experienced a delay to their diagnosis had increased stress, anxiety, and feelings of isolation.
- Missed opportunities for early intervention: timely diagnosis of Alström Syndrome is crucial for implementing appropriate interventions and management strategies.
- Lack of research and treatment advances: the lack of awareness about Alström Syndrome can contribute to limited research efforts and funding for the condition. Insufficient research and treatment advances can further impede the diagnostic process and limit access to therapies or clinical trials, ultimately impacting patient outcomes.
- We can therefore not stress enough the importance of awareness raising and improving the knowledge and understanding of healthcare professionals.

The role of ASUK and similar patient organisations, is critical to this. Our findings have demonstrated that in many cases, ASUK are the first touchpoint by patients and their families when seeking more information and support following a diagnosis. However, this is often dependent on the patient or parents' skills and abilities to do their own independent research and their confidence to reach out.

Health Equity

A report published in 2022 by The NHS Race and Health Observatory[2], gathered evidence to illustrate the significant ethnic inequalities in healthcare. Findings show that people who are from diverse and marginalised communities and affected by a rare/genetic condition, often experience a huge disadvantage in areas such as genetic testing, mental health, and access to healthcare services. Our research has identified similar findings - we noted a considerable variance in the 'patient experience' in terms of access to quality, effective care, and the speed of diagnosis. This variance of ethnicity, education level, awareness, accessibility, and patient place of residence appears to demonstrate further barriers to a timely diagnosis.
All these factors had a significant impact on patient outcomes.

Impact of patient location

Patient 4, based in a rural and remote area of the UK, where expertise in AS, or rare conditions in general, may be limited, resulted in a particularly challenging journey to diagnosis. Parents feel they received sub-standard medical care from their local hospital due to a lack of consistency and the availability of medical staff with specialist skills to provide effective treatment and appropriate referrals.

The family spent many months visiting their local hospital, each time seeing different medical professionals and being given conflicting information about their child's health. Only due to the persistence of the parents, was patient 4 referred to a larger hospital to be assessed by appropriate specialists. It was at this hospital that the patient was finally diagnosed.

Impact of patient ethnicity/culture

One family shared their uphill struggle in seeking a diagnosis. Their journey was delayed and their relationship with healthcare professionals was poor. Sadly, this family felt they were at risk of being blamed for their child's condition. Parents are related by blood and are well aware of the stigma surrounding consanguinity. Due to their lived experience and the lack of cultural competence amongst the healthcare professionals involved in their care, parents do not feel that engagement and communication was positive. Therefore, they have opted out of having genetic testing (although their child has received a clinical diagnosis).

Appendix 1. Showcases the development of a Framework of Culturally Competent Genomic Care, developed by the Yorkshire Regional Genetics Service.

Impact of Education and Awareness of healthcare professionals

As explained in section 2.6 many of our families experienced disappointing levels of awareness, knowledge, and expertise in AS amongst healthcare professionals and as a result, this had a negative impact on their journey to diagnosis.

Recommendations and Actions

Targeted education and training are critical for increasing awareness of AS and other rare conditions. Healthcare professionals should be encouraged to 'Think Rare' and be aware of red flags such as unusual symptoms and multiple appointments. Continually evaluating and updating current AS clinical guidelines can help with the dissemination of information to support healthcare professionals to link symptoms and understand the referral criteria for genetic testing. Standardised protocols can help to achieve equity of access. When it comes to genetics, there needs to be a clear structure on what type of tests should be requested depending on the circumstances. Adopting a multidisciplinary approach improves collaboration and should involve the various specialists involved in a patient's care ([3],[4]).

In this digital age, lack of access can no longer be an excuse. The use of virtual consultations can help bridge this gap between symptom onset and diagnosis, especially in areas with scarce access to specialist services. Having comprehensive assessments can minimise error and avoid incorrect conclusions ([5]). A rapport of trust and openness between families and clinicians can alert healthcare professionals to certain concerns and observations enriching the patient experience. Having a holistic approach can help identify and support the social, emotional, mental and physical impact of AS.

Growing interest in AS could result in more research that could lead to developments such as clinical trials and therapies ([6]). Publications highlighting where cardiac transplantation has been successful could provide scientific evidence that could influence decision making and provide lifesaving procedures for patients. NHS England could endorse charities such as ASUK to provide reassurance, support and encouragement to healthcare professionals to signpost newly diagnosed patients and families. Mandatory training on cultural competence and humility is a practical solution to help meet the needs of our diverse community and to help understand the impact a patients' background can have on their health outcomes and access to services ([7]). The BDB Experts by Experience Advisory Group are a diverse group of people living with rare conditions. They provide support to the BDB network by sharing their experiences to improve understanding and help guide the development of organisations and services.

Liaising with healthcare professionals to raise awareness of the main symptoms of AS may help identify people who are yet to receive a diagnosis. Exploring the possibility of AS being included in newborn screening would be gold-standard for accelerating diagnosis ([8]). Lessons learned from the past should be reflected on moving forward if we are to create the best chance of diagnosis for all people with AS.

Recommendations in practice

1. Targeted and widespread training and awareness

- It is unrealistic to think healthcare professionals will learn about all 8,000 + rare conditions but could be encouraged to 'Think Rare', when presented with multiple or unusual symptoms. Therefore, mandatory training for healthcare professionals on how to **'Think**

Rare', using resources developed by [9]Medics 4 Rare Diseases (Rare 101) and Health Education England's Genomics' Education Programme (GeNotes)[10] is crucial.

- Mandatory training on developing cultural competence and humility to promote positive cultural communication delivered to healthcare professionals.
- To use established models such as 'A Framework of Culturally Competent Genomic Care' (see appendix 1).
- Learning from initiatives such as the culturally competent genomic medicine service for underserved groups in areas of high need – findings to be shared with healthcare professionals throughout the country with specific actions to improve competence and accessibility of Genomic Medicine Services.
- Healthcare providers to be made aware of and learn from the UK Rare Diseases Framework[11] and each of the nation specific Action Plan's and progress updates.
- The UK government and delivery partners to continue to engage with the rare disease community to further develop new and improved actions to address the priorities within the UK Rare Diseases Framework[12], including 'Getting a final diagnosis faster'.

2. Highlighting the first 3 key symptoms of AS

- Widespread training around the overall clinical features of Alstrom Syndrome.
- Targeted awareness of the 3 main symptoms as detailed in this report - obesity, sight loss and cardiovascular disease.
- Raising awareness of AS and the highly specialised clinical service with all paediatric weight management clinics, cardiology and ophthalmology departments and promoting genetic testing.
- Regular updates to the AS clinical guidelines and dissemination amongst healthcare professionals.
- Produce a publication to highlight the success of cardiac transplants in paediatric patients diagnosed with AS.

3. Development of clinical and diagnostic pathways

- AS to be included as part of NHS newborn screening.
- Explore the possibility of AS being added to the list of conditions included in the Generation Study.
- Equitable access to genetic testing – clear guidelines around when to do single gene, panel

testing and whole genome sequencing.

- Access to diagnostic guidelines which clearly outline the specific clinical features and diagnostic criteria required for suspicion and referral for genetic testing. Establishing standardised protocols can also help minimise diagnostic errors and ensure consistent evaluation across healthcare settings.
- Improving collaboration - adopting a multidisciplinary approach to diagnosis, involving all specialists involved in a patients care.
- Communication - open and collaborative communication among those involved in the care of AS patients helps to facilitate the sharing of clinical information, test results, and observations to provide a comprehensive evaluation and avoid isolated assessments that may lead to incorrect conclusions.
- Improving the visibility of the AS highly specialised service.
- Supporting healthcare providers to understand the referral process and their responsibility to refer patients in a timely manner.
- Establishing clearly defined clinical pathways – including specialist and local healthcare providers, tests, monitoring and support.
- Further investment in mental health services to support patients and families.
- All stakeholders need to understand the important role that patient organisations play in supporting people living with rare conditions.
- A further detailed analysis of the journey to diagnosis which combines patient/parent/carer experiences with information from health care professionals and examines healthcare records.
- Exploring the journey to diagnosis within the wider BDB network.

4. Development of genetic support services

- Genetic test results should be shared using plain language with access to genetic counselling and signposting for further support.
- Endorsement from NHS England to highlight ASUK as a reputable source of information and support so that healthcare professionals feel confident to signpost patients and families.
- Better utilisation of virtual consultations to facilitate early assessment, diagnosis, and appropriate referrals - especially in areas with limited access to specialised medical care.
- Improve patient and family involvement: engaging patients and their families as active

participants in the diagnostic process and encouraging them to share their concerns and observations can contribute to a more accurate diagnosis.

5. Involving people with lived experience

- Involving people with lived experience in the development of services and the co-production of resources. ASUK to facilitate access to the BDB Experts by Experience Advisory Group to provide guidance and consultation.
- Promote patient and public involvement and engagement – being as diverse and representative as possible and including the voices of people who often go unheard.

6. Encouraging organisations to join the BDB network

- Increasing the visibility of Breaking Down Barriers and encouraging all stakeholders to join and work together to improve engagement and involvement with people from diverse, marginalised and underserved communities who are affected by rare and genetic conditions.
- BDB to provide training on the importance of addressing Equity, Diversity and Inclusion and helping to understand how health inequalities have a negative impact on health outcomes and access to services.

Conclusion

It is important to learn from patients and their families' experiences of diagnosis and to understand how these experiences impact their health outcomes and quality of life. Findings in this report highlights where some of the gaps are and areas within the health service that requires improvement. It also helps us to identify the areas of good practice and find ways to build on this to improve diagnosis and care pathways for people living with Alstrom Syndrome.

The role of ASUK and similar patient organisations, is critical to this. Our findings have demonstrated that in many cases, ASUK are the first touchpoint by patients and their families when seeking more information and support following a diagnosis. However, this is often dependent on the patient or parents' skills and abilities to do their own independent research and their confidence to reach out. This contributes to the health inequalities experienced by people from diverse, marginalised and under-served communities. If we are to achieve equitable access to services and support for all then more needs to be done to improve care pathways and the structure and accessibility of services and support.

We acknowledge there are limitations to this report, firstly our sample size is inevitably small due to Alstrom Syndrome being an ultra-rare condition. While this report focusses on the experiences of patients and their families; speaking to healthcare professionals and having access to

healthcare records would have allowed us to explore issues such as the route to diagnosis, causes of delays and the impact of an early diagnosis on the suitability for cardiac transplantation in more detail. We would then also have a greater understanding of the experiences of healthcare professionals, the barriers, and limitations within healthcare services and to explore possible solutions. With this in mind, ASUK would welcome the opportunity to collaborate with patients and their families and with the healthcare professionals involved in their care to further explore, learn, and find ways to improve the journey to diagnosis.

We would also like the opportunity to do a similar research study with the BDB Network, which is made up of 70+ rare disease organisations – this could expand on the study sample and provide a more detailed overview of the diagnostic odyssey for families diagnosed with rare conditions.

Thank you to all individuals and families who gave their time and shared their insights to contribute to this report. We hope these findings will help improve services for future families in their search for answers on their journey to a diagnosis.

Please do get in touch if you are interested in finding out more information about this work or to discuss opportunities for further collaborations.

Thank you

Family Stories

Teddy's journey told by his dad

Birth

When Teddy was born there was nothing to suggest that he had a condition or any concerning symptoms. Teddy was six pounds and 5 five ounces and his hearing and eyes, after a check by the hospital, were confirmed to be fine. On discharge the only notable condition on Teddy's notes was that he had a Mongolian Blue Spot.

After Teddy was discharged from hospital, he gradually started to gain weight and although I noticed he was becoming quite a big baby I wasn't initially concerned. Family members reassured me that I was also a big baby, and that Teddy would likely lose a bit of weight once he became physically active and started to crawl. I remember Teddy feeding a lot and drinking lots of powdered milk. At the time I thought this could have been a culturally motivated decision, on behalf of Teddy's family members, to 'feed up' Teddy which, from a cultural perspective, is seen as a way of showing affection.

Hand-eye co-ordination

Up to the age of 1 and before becoming very mobile, Teddy had good facial expressions, enjoyed engaging and had a great sense of humour. His eye contact and hand-eye coordination was also good. I distinctly remember Teddy used to enjoy playing with a spinning top, grabbing it, playing with it and pushing the buttons.

Trigger Finger

At some point before Teddy was 1 year old, I noticed that he started to have difficulty bending his thumb, it looked stiff and in a locked position when we used to play together. I noticed Teddy would have difficulty with certain activities so just before his first birthday Teddy was admitted to hospital for surgery to repair the tendon in his thumb. Trigger finger was the final diagnosis which is quite a common condition that causes the tendons in fingers to become swollen and inflamed.

Hospital Admission (Apr 15-Apr 16)

Between the ages of 1-2 years old, I can't quite remember the exact point, Teddy developed quite a severe cough and after trying to treat Teddy's cough at home and a trip to the GP, he was eventually admitted to hospital. During his hospital stay the Doctors raised their concern about Teddy's weight and said that he was obese. The concern was so great that Teddy remained in hospital while investigations and tests were conducted to try and establish a clinical cause for his obesity. Teddy made a recovery and was discharged from hospital, a cause for his obesity was not found but he remained under the supervision of a Community Paediatrician.

Neurodevelopment

Between the ages of 2 and 3 years, Teddy's speech development was exceptional. His speech was eloquent, articulate and engaging. However, Teddy's social development started to fall behind his peers. Teddy struggled to engage and play with other children and became frequently angry. I also noticed he would flap his hands a lot. After monitoring Teddy for some time, by December 2017 (when Teddy was 3 years old) I reached the conclusion Teddy could be autistic. Following this I sought a neurodevelopmental assessment and Teddy was subsequently diagnosed with Autism Spectrum Condition and sensory processing difficulties.

Vision

When Teddy was born, I didn't realise he had a vision impairment. It wasn't until I noticed he wasn't reaching for things, and then when he started to crawl and walk, he would bump into things. Between the ages of 2-3 years, I organised for Teddy to have his eyes tested, initially he was diagnosed with nystagmus and photophobia. Teddy's eyesight continued to deteriorate and by the age of 5/6 he was diagnosed with Macular Dystrophy and registered severely sight impaired. It was during an eye appointment that I was first introduced to Guide Dogs UK. At the time I didn't realise all the services that Guide Dogs offer for children and families, but I reached out to them nonetheless. They were very supportive and knew the best way to help Teddy was to also help me. It was with the support of Guide Dogs and their specialist education team I was able to fight to get Teddy the Education Health Care Plan he needed.

Autism Diagnosis

It was in the summer of 2018 (when Teddy was 3 years old) that genetic tests were first considered. Blood samples from me, Mum, and Teddy were taken, and results were initially inconclusive. Someone suggested Bardet Biedl Syndrome and they did a specific test for that, but nothing came back positive. There was a potential variation on the APPCA41 gene, but they weren't sure if it was a regular variance or something more sinister and they looked specifically for that but weren't sure. We were then referred to the 100,000 Genomes Project which conducted further genetic tests on Teddy.

We waited until March 2020 for the test results to come back and were sent a letter scheduling a 45-minute conversation with the genetics team. During the phone call it was confirmed Teddy had the ALMS1 gene mutation, meaning he had a diagnosis of AS and Teddy has since been referred to the Birmingham specialist AS clinic.

'You were the first person I properly could talk to about your son's experience to try and give me some understanding of where I'm at? is it enough? could I do more? what do I need to do next? instead of just lurching in the dark.'
(Teddy's Dad gives his experience of being supported by ASUK)

Ella's journey told by her Mum

Background & Birth

Ella was born via an elected Caesarean on 2nd August 2016. Ella's birth weight was 5 and a half pounds.

Vision (birth to 2 years)

Once Ella was 3 months old, we started to notice her eyes were struggling to focus and she was seen by the GP and by a locum doctor in our local hospital. However, it wasn't until Ella was 6 months old, when she was admitted to hospital with bronchiolitis, that she finally received a referral to an Ophthalmologist. A nystagmus diagnosis followed at 7 months old, and we were told this could be managed by our local hospital. Between the age of 7 months and 2 years we were told Ella's nystagmus was caused by a high refractive error, but her vision continued to decline. Ella began to withdraw from the world and failed to meet her expected milestones for crawling, walking and speech.

At this stage no association was made between Ella's poor vision and mobility difficulties. I wasn't happy with the care Ella was receiving in our local hospital and sought a referral to Ophthalmology at a larger and more specialist hospital.

They prescribed glasses for Ella which helped, however, her vision continued to decline. At the age of 2 years and 10 months (June 2019) the hospital conducted an electrodiagnostic test and Ella was subsequently registered blind. Ella found this appointment, and those leading up to it, very distressing. She had become uncooperative and extremely anxious whenever she had to go. Long distance journey to appointments didn't help this. We consequently decided to pause check-ups and investigations until Ella was more able to cope with the tests that needed to be carried out. Doctors advised us that this would not hinder the management of Ella's vision impairment and probably a good idea as tests were becoming increasingly difficult to perform and achieve accurate results. Had we known Ella's symptoms suggested a possible genetic condition we would not have taken this decision. We felt ill advised.

Weight & diet

As a baby Ella had a lot of feeding issues, at 20 days old she was diagnosed with reflux oesophagitis which caused the contents of her stomach to reflux into her oesophagus. This made it incredibly difficult for Ella to feed and worried us. Feeding problems persisted and it wasn't until she was admitted to hospital with bronchiolitis at 6 months that we received some advice about how to manage it. Ella was then put on hypoallergenic formula which unfortunately she didn't take to very well. Eventually the GP made a referral to a consultant paediatrician, and at age 1 year old Ella was diagnosed with an allergy to cow's milk.

Sadly, Ella is not very active due to her poor vision which causes her to be unsteady on her feet and to lack confidence when mobile. Ella frequently bumps into things.

I don't think Ella's weight is a huge problem and I would describe her as mildly overweight carrying most weight around her tummy. Ella has slim legs.

Ella does not have excessive hunger and follows a low carb diet due to her food intolerances.

Gross Motor Skills

At 17 months old Ella was seen by the community paediatrician, during this review the doctor noted a gross motor delay, but no link (at this point) was made between Ella's poor mobility and vision issues.

Ella's joints are extremely flexible, and she has been diagnosed with hypermobility. Her knees and ankle's role when she walks, so she's had to have a lot of physiotherapy. Ella has flat feet, and it is very difficult to find shoes that fit.

Ella was offered an MRI to investigate her gross motor delay, but we decided to decline this as we didn't want to expose Ella to any unnecessary health consequences.

Speech and Language

Once Ella reached the age of 2, we became concerned she had a speech and language delay. It was at this time we also requested an autism assessment for Ella although she didn't 'fit the profile' for autism. Although Ella has difficulty expressing herself and only has a very limited vocabulary, she does not appear to have a receptive language deficit and understands everything that is being said to her.

Ella receives speech therapy but as, yet her language skills have not progressed as much as initially hoped. I think it is difficult for speech therapists to support patients with vision loss and this is part of the problem.

A tool for speech therapy assessment is observation during imaginative play and Ella has never done 'pretend play'.

Hearing

Ella's hearing, 'seems good on the face of it'. Between the ages of 2-3 years Ella had a number of hearing tests which were inconclusive because she wasn't conventional in terms of how she responded to the sounds. If she heard something, she would go quiet and still, she wouldn't turn and look for a noise. Ella had a hearing test in June 2022 and there was a question mark around whether she could hear all pitches. I feel that Ella's vision loss is impacting what she hears as she is not able to lip read.

Diagnosis

In August 2021 Ella attended a routine check-up with the Ophthalmologist. During this appointment the Consultant noted bilateral reduced vision, high hypermetropia, small crowded optic discs, reduced retinal function and nystagmus. He also noted suspected oculocutaneous albinism and referred Ella for genetic tests.

In May 2022, we received a letter from the Ophthalmologist confirming that as a result of Ella's genetic tests, Alström Syndrome had been identified. Sadly, no support or correct signposting or an appointment to discuss the diagnosis was offered to us within this letter.

In the absence of appropriate support, we conducted some independent online research of our own to find out more about the condition. It was this online search that led us to ASUK who has since ensured we are connected to the right professionals for support and put on the list to attend the specialist AS clinic in Birmingham.

Vision (Age 2 to 6 years)

Ella is now registered blind, and she wears prescription glasses which are regularly adjusted, and she has tints to protect her from very strong sunlight.

Education

Ella started nursery at a mainstream primary school in September 2019. Although they were initially supportive, it became increasingly difficult to get the right support for Ella even though she seemed very happy there. She stayed for 6 months and then we decided we had no choice but to remove her due to the lack of appropriate care for Ella's very specific needs.

In January 2022 Ella started a specialist school 22 miles from home and we have managed to secure 1-2-1 support for her while she is there. Guide Dogs and RNIB are key organisations supporting Ella's transition to a new school which has really helped.

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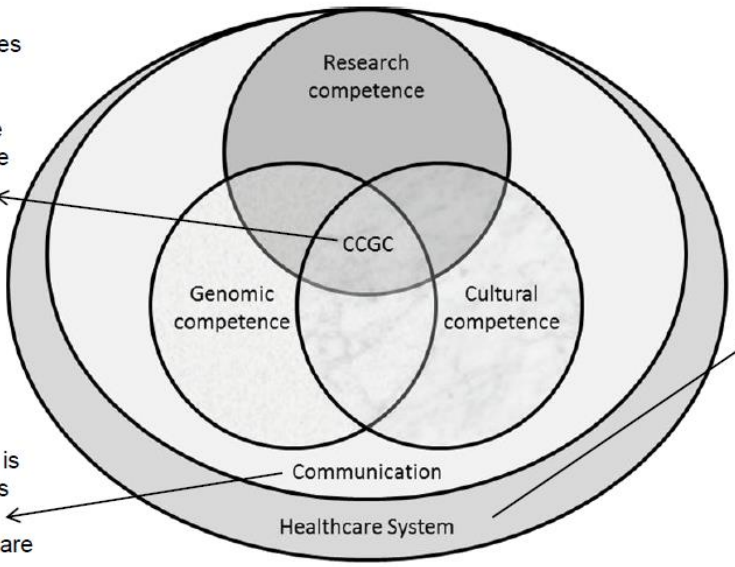
Appendix 1.

A Framework of Culturally Competent Genomic Care (CCGC)

This framework comprises three core concepts:
- Cultural competence
- Genomic competence
- Research competence

The area of overlap between the three core concepts ensures safe, ethical, and effective clinical practice in the delivery of CCGC



The healthcare system plays multiple roles within this framework:
- Developing culturally competent strategies that help to engage diverse populations in genomics
- Workforce training
- Provision of resources for genomic education and cultural competence training

Effective communication is the central concept of this framework, in which the three core competences are embedded

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Yorkshire Regional Genetics Service

The Leeds Teaching Hospitals NHS Trust