

findacure

Rare disease perspectives
2016



Patient focus group report: Wolfram syndrome

This study was completed in the first half of 2016, as part of Findacure's Drug Repurposing for Rare Diseases Social Impact Bond Development project, with the assistance of Birmingham Children's Hospital, Wolfram Syndrome UK and WellChild.



LOTTERY FUNDED

The cover image does not depict an actual focus group event, rather showing another Findacure meeting. The identity of all focus group panellists is purposely kept private.

All of the information in the following report is based on the facts, examples, and opinions expressed in the Findacure focus group. Findacure would like to thank all members of the panel for their valuable participation and insight. We also thank Birmingham Children's Hospital's Wolfram clinic team, Wolfram Syndrome UK, and WellChild for their help in organising this focus group.

Executive summary

Wolfram syndrome is a rare genetic disease which affects patients from childhood. The disease is characterised by dilute urine, diabetes mellitus, severe visual impairment, deafness, and neurodegeneration. Findacure ran a Wolfram syndrome patient focus group to assess the current treatment and care available to patients, the cost of the disease to affected families, and the patient perspective on clinical trials. The major findings from the focus group, which are detailed below, were used to build an argument for the need for new treatments for Wolfram syndrome, potentially funded by Findacure's rare disease drug repurposing social impact bond.

- ❑ Wolfram patients and families think highly of the Wolfram clinic at Birmingham Children's Hospital. This provides good support to patients, and allows clear communication about the disease and its progress. The clinics can be tiring and stressful at times, but are appreciated.
- ❑ Families are desperate for a treatment and there is a huge need to slow disease progress. Generally, patients are most concerned about the most isolating symptoms – the loss of sight and hearing – but experiences do vary widely in the Wolfram population.
- ❑ The Wolfram clinic and Wolfram syndrome annual conference provide strong lines of communication between the patients and clinical researchers. While communication of complex science can always be improved, this connection is highly valued by the Wolfram community and helps to provide a source of hope about future clinical trials.
- ❑ The cost of care is very high for Wolfram families, with particular difficulties experienced in securing the required support in the education system, particularly due to the gradual degenerative nature of the disease.
- ❑ The emotional impact of Wolfram syndrome on families, and particularly patients, is hard to overstate. The disease is experienced differently by all patients, this varied experience, combined with the isolating nature of sensory degradation, can make it hard for patients to find people with similar life experiences.

Rare disease perspectives

In late 2015 Findacure secured a development grant from the Big Lottery Fund's Commissioning Better Outcomes Fund in order to investigate the potential of a social impact bond to provide a new source of funding for generic drug repurposing in rare diseases. As part of this proposal, Findacure wished to engage with rare disease patients, in order to gain a better understanding of their need for new treatments, and the issues they deal with on a day to day basis.

To achieve this, Findacure decided to run a series of four patient focus groups, to collect the perspectives of rare disease patients. These focus groups helped to provide the personal stories and patient opinion crucial to build a strong argument for the underlying need for Findacure's proposed drug repurposing programme. The first of the focus groups gathered rare disease patients and advocates from across the spectrum. The other three groups were disease specific, focusing on the three rare diseases which formed the focus of Findacure's health economic studies: congenital hyperinsulinism, Wolfram syndrome, and Friedreich's ataxia.

The completed focus group reports have been made available to all of our anonymous focus group participants, our clinical partners for each of our rare diseases, and our patient group partners. They also form a key component of our final presentation to the NHS, designed to discuss the potential of commissioning a rare disease drug repurposing social impact bond to deliver new treatments to rare disease patients in the UK.

Wolfram syndrome

Wolfram syndrome is a rare genetic disease, characterised by diabetes insipidus (dilute urine), diabetes mellitus, severe visual impairment, deafness, and neurodegeneration. The symptoms develop in early childhood, diabetes mellitus being the most common early sign, followed by degeneration of the eyesight around the age of 10. Patients report everything "going grey" initially, with severe visual impairment by the late teenage years. Many Wolfram patients die prematurely, however there is great variation in the presentation of the disease, and improved care and understanding has enhanced patient prognosis in recent years.

In early 2016, Findacure attended a Wolfram clinic at Birmingham Children's Hospital, and were able to meet a number of patients and families. We conducted a short focus group over lunch in order to better understand:

-  the need of Wolfram syndrome patients for new treatments
-  what Wolfram patients need from a clinical trial
-  the financial burden of Wolfram syndrome to families, and its social and emotional impact

The report below summarises the information gathered from this focus group, and a number of subsequent conversations from Wolfram families. All participants consented to be involved in this study, and have been informed how their thoughts, experiences and opinions will be used.

Current treatment

Journey to diagnosis – Prior to the focus group, Professor Tim Barrett outlined the most likely route to a ‘quick’ diagnosis of Wolfram syndrome, which was exemplified by one of the families. The patient was diagnosed with diabetes at the age of five, with the condition managed by local doctors and the family. Further investigation was only undertaken after vision began to deteriorate. A high-street optician noted visual deterioration one year after a perfectly normal eye check and referred the patient to the local hospital for further investigation. They made the connection between diabetes and deterioration of eyesight. Roughly four months of numerous tests and referrals led to a Wolfram syndrome diagnosis and attendance of the Wolfram clinic at Birmingham Children’s Hospital.

“I think everyone is an individual and I want people to see me for who I am and not as my condition.”

– Wolfram patient

In stark contrast, another of our families had a much harder route to both diagnosis and treatment. In this case the patient presented with diabetes at the age of three, with eyesight deterioration first noted between the ages of five and six. Unfortunately, the connection between the symptoms was not made – it took another six years for the diagnosis of Wolfram syndrome to be reached. Even with this diagnosis, the patient was not referred to the specialist Wolfram service until the age of 17. Prior to this his symptoms were monitored and managed independently by different specialists locally.

There is great variation in diagnosis time for all families that we spoke too, which is compounded by the variability in disease presentation. For patients presenting early with hearing loss or breathing problems (both of which are less common at a young age), a Wolfram diagnosis is slower. One adult patient took over thirty years to secure their diagnosis, primarily because they never presented with diabetes mellitus – one of the most common symptoms. Generally diagnoses take around three years following the appearance of diabetes mellitus and a second symptom. For the patients we talked to, a single clinician who happened to wonder about the connection between the different problems reported by the patient was invariably key to securing the diagnosis. The importance of frontline clinicians taking the symptoms of patients seriously, and pursuing them, cannot be overstated.

Existing treatment – For many patients the Wolfram clinic at Birmingham is the only place where they can see clinicians with any experience or expertise in the disease. Currently the paediatric clinic provides a comprehensive multi-disciplinary team to manage the disease – ophthalmology, urology, neurology, psychology, genetics, and hearing are all addressed. The adult clinic is less comprehensive, but does include endocrinology, genetics, and psychology. Any treatments are targeted at specific symptoms (e.g. desmopressin for diabetes insipidus), as no disease modifying treatment exists. Patients should attend the clinic annually. Outside of this local treatment is more varied, but should ideally be guided by clinic letters sent to both families and local doctors. Unfortunately this process is not always as smooth as it could be, either due to administrative failures or a reticence on the part of local clinicians to follow clinic recommendations.

Local treatment will depend greatly on symptoms and disease progress. In general, patients seem to have quarterly check-ups with a consultant endocrinologist for diabetes management during childhood. These may drop to twice annually as they move to adult care. Other specialisations are generally seen annually, including opticians, urologists, and hearing specialists. Those patients presenting with breathing difficulties, in need of a tracheostomy, are likely to have an annual bronchoscopy. Other services, such as sleep studies, psychiatry, or orthopaedics for scoliosis, are engaged at need on a more ad hoc basis. At least one of the patients we talked to has had over three extended blocks of counselling to help deal with anxiety linked to the disease. Adult patients often

collect their own team of local specialists around them, who are contacted every year to 18 months. These may include a range of other treatment areas such as podiatry and bowel specialists.

Experience of the clinic – The paediatric Wolfram clinic has a big impact on both patients and their families. One parent described the service as a “full health MOT for Wolfram patients”, while another described it as “a heaven”. As the parent of a newly diagnosed child, the clinic provided the answers to all of their unanswered questions, allowed direct conversation about the disease, and helped them to deal honestly with their child’s questions. All families felt that they were given time and attention to address to broad spectrum of Wolfram needs. One patient remarked that there is a different experience between the Wolfram clinic and local care. Locally, appointments were slow, and he did not really know what was going to happen both during treatment and in his future.

However, it is important to note that the intense nature of the clinic can be stressful for families and particularly patients, given their tendency towards anxiety. Seeing so many specialists in such a short time is both a unique opportunity and a gruelling experience. For older children it can also divert their focus from day to day management of symptoms to the bigger picture of the disease. This can quite naturally lead them to wonder ‘what will go wrong next?’ and worry about their future. This is certainly a problem that will persist for the clinic while there are no real treatments available.

“I find it quite hard to come to terms with the condition as I don’t really think much about it outside the clinic.”
– Wolfram patient

It is due to this that the clinic’s research involvement was important to parents and older patients alike. It is a source of hope and gives them a chance to increase their understanding of their disease, and hopefully improve its management and treatment. Patients are keen to be involved in trials and seek out opportunities to learn more about current research.

Treatment hopes and aims

New treatment need – For the majority of patients we spoke to a treatment that could address their gradual loss of sight was a priority. The loss of sight is scary, stressful, and greatly impacts the lives of patients. They realise that the damage to the eyesight is currently irreversible, so any treatment to slow deterioration is crucial. However, some older patients, who experience both sight and hearing loss felt that hearing became the biggest issue: loss of hearing cut them off from the people around them and was an exceptionally isolating process. It is important to note again that the variation between patients is huge, for example, one adult patient cited bowel problems as the most concerning in their life. Given this variability, any treatment which targets the underlying cause of the disease, and could halt further progression, would clearly be appreciated. The families felt the time pressure of the disease – while the progress can be slow, it is relentless. They were desperate to quickly see a treatment that could at least slow, if not halt, degeneration.

The patient perspective on clinical trials

For many families clinical trials represent hope – they see a future of blindness, deafness, depression, and respiratory struggles. The prospect of a disease modifying treatment is their main hope to delay or avert this future. This hope helps to provide focus and motivation, as well as combat depression in patient and parent alike. One parent spoke candidly about their own battle with depression after their child’s diagnosis – knowing that researchers are working to help Wolfram children proved key to beating this.

"Everyone is desperate for a treatment. I would do anything for my child to be involved in a clinical trial"

– Wolfram parent

When questioned about their willingness to be involved in trials, families were unanimous in the view they would commit as much time, effort, and money as they were able to be involved. One spoke of relocating closer to the trial centre. Financial support to mitigate against loss of work, travel costs, and accommodation would clearly be appreciated, and be likely to help families remain part of the trial. They saw trial participation as not only a chance to help themselves and their families, but as beneficial to the next generation of Wolfram patients. Patients, particularly young patients, can find it hard to take part in research though – the science is complex and studies stressful. While they recognise its importance and potential, it does carry a burden.

Families also felt that information about trials and research was crucial. They want to know that they 'are part of the project'. They appreciate hearing anything about current research, whether in consultation with the Wolfram team or at the Wolfram Syndrome UK annual conference. It is important to them that researchers are as open as possible. More than this, however, it is crucial that the communication is as clear as possible, so that it is accessible to all of the families. The current Wolfram researchers are viewed positively in this regard. They always aim to make their research understandable (though work can always be done in this area) and are very open, regularly sharing research successes and, equally importantly, failures. In particular the Wolfram syndrome annual conference (cofounded by Wolfram Syndrome UK and WellChild) is very well regarded, giving patients a chance to meet one another, as well as a place to interact with researchers. The research talks can be viewed as scientifically "heavy" at times, but are appreciated. Patients want to see the progress, problems, and plans explained in as simple a manner as possible. They know that this is something that is continually improving and would hopefully develop further in a clinical trial setting.

The burden of Wolfram syndrome to patients and families

Financial costs - For many Wolfram families a major financial cost comes through loss of working hours. Without an understanding employer, the need to take time off work to constantly visit clinics and specialists can threaten parental employment. In one family we spoke to, one parent became a carer full-time for the best part of ten years. Another parent had to sign off work for six months to care for a patient after a tracheostomy. There is a persistent accumulation of lost work hours for parents, whether through repeated hospital appointments or the need to support their children at school. This type of burden of care is particularly difficult for single parent families, and with the degenerative nature of Wolfram syndrome, it is a burden that increases throughout life.

Due to the high care burden, Wolfram families generally receive a number of different benefits from the government. Patients usually receive disabled living allowance, while families will often secure carer's allowance. In adult life some patients will receive PIP (personalised independence payments). Respite care is also used, when it can be accessed. One family said that they received it three nights a week, while another had to secure direct payments to fund it. Dependent on income, some families may also secure reductions in council tax, water rates, and TV licences. As patients get older they are likely to need specialist support for transport to college and doctor's appointments, disabled student allowance, mobility training, and equipment. They may also struggle to secure work, depending on disease stage, leading to further benefit payments. Those that take up work often have to retire early, with uncertainty over how they will maintain their independence in later life.

Other direct costs to families include travel costs to specialist centres, which one adult patient reported at over £100 per trip. All hospital appointments have associated costs, as well as accommodation for family members if needed to support patients during visits. Attendance of the Wolfram conference adds an additional need for travel and accommodation, though this is subsidised by WellChild. Some patients may also have to pay for over the counter therapies to manage things like acid reflux, which can be quite severe and lead to dental erosion without medication.

One family reported that parental depression, an illness reported by a number of families, added a financial burden both through loss of work and the cost for therapy. This can also put great emotional strain on relationships.

"You know, everyone wants a life when they grow up, everyone wants to get married."

– Wolfram patient

Emotional cost – For patients, the gradual loss of senses can have a profound emotional impact, which is often linked to feelings of isolation and depression. The combined loss of hearing and vision can be profoundly isolating for patients, while a knowledge of possible disease progression clearly increases anxiety. Even from a young age diabetes can act as a barrier to a social life; one father reported that his child received less party invites from a young age, due to their special diet and the need for glucose monitoring. This type of exclusion could have heightened a sense of isolation and harmed confidence.

The emotional cost is high to parent and patient alike. Parents often suffer severely from depression once their children are diagnosed. Patients themselves are also prone to depression and anxiety. These are notoriously difficult conditions for which to secure treatment, though the paediatric Wolfram service at Birmingham Children's Hospital does provide support for this and psychologists are also part of the adult service. Patients often receive multiple blocks of counselling throughout their lives, though these remain difficult to access and are often delayed.

Patient groups can provide some support for both patients and parents – shared experiences providing a source of understanding, and people with whom they can relate. However, there is great diversity in the disease and patient's experience of it, which can limit the usefulness of these groups for some individuals. Others relish the help and support provided through patient networks.

Schooling – There is a big cost to the education of Wolfram patients, due to their need for sensory support, glucose monitoring, and other specific needs. These are likely to increase as the disease progresses. Schools have to be able to support children with glucose monitoring and provision of insulin injections (if required) due to patient diabetes. Eyesight will degenerate throughout school life, meaning that pupil visual needs have to be taken into account early in life and monitored closely. Hearing may deteriorate for some patients and bladder control may be poor.

In the UK, patients should have a special education plan in place, but this is often hard to obtain or hard to enact. One patient we spoke to had never had a special educational programme or any real support. He felt that schools struggle to understand the problems that kids have, their needs, and how to cope with them. Provision of support seems to vary widely between schools or regions, and some parents have had to fight schools and LEAs for the support that the children need. This adds another layer of stress and pressure to parents already learning to cope with the needs of their kids and to kids trying to cope with their illness in a school environment. Despite preparing a new school for their child's needs six-months prior to the start of the school year, one parent spent eight weeks training staff to care for their child, and was expected to be present in all classes during this time. Despite this

huge effort, she was asked to remove her daughter from school a few months later as her needs were, apparently, too great. Educational experience is hugely influenced by the outlook of individual schools.

Diabetes is a major problem for most children at school. Symptoms are hard to manage and necessitate special training for teachers. If this is not given, it can exclude kids for sports activities or field trips that they are completely capable of being involved in. Parents have had to step-in in many cases to help with diabetes management in these situations. Such constant parental supervision is clearly not ideal for Wolfram patients as they get older. Patients also lose class time due to diabetes.

"They [Wolfram patients] can do something, they can be someone, but they need helpers."
– Wolfram patient

One patient told us that he finished school when he was 16, prior to completing GCSEs. His school could not meet his needs: his blood sugar never stabilised, leading to multiple collapses at school, which prevented him continuing his education. He had no help at all from school. He said that he felt that education is lost to him without further help. He requires lessons in braille due to the severe degeneration of his vision – something he would like and the Wolfram clinic may be able to source for him. In contrast, another patient had a much better experience of the school system. Their school was open and willing to help manage patient diabetes, with teachers receiving special training.

Conclusions

Wolfram syndrome has a huge impact on the lives of families and a devastating effect on the patients. It incurs significant psychological cost to all involved and its gradual degenerative nature, particularly during school years, has a huge impact on education and social confidence. There are substantial costs to the government incurred from both health and social care. Patients and families can only benefit from a more joined up approach to health and social services, helping to deliver the care that patients need throughout life, as well as support for parents.

Any new treatment with the potential to slow or halt disease progression would have a huge impact of patient health and quality of life. It would improve education, increase self-reliance, and reduce both healthcare and social care spending, especially if delivered early in disease progression. Crucially, halting or slowing disease progression would help to secure an increased level of independence for adult and childhood patients alike.

