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THE LIFE EXPERIENCE OF aHUS PATIENTS,THEIR FAMILIES AND CAREGIVERS IN ENGLAND AND WALES

1. Introduction

This report describes life with aHUS and how the disease affects patients, partners and family members. It focusses on current diagnosis and treatment, rather than providing a historical perspective on how disease management has changed over time. The report is based originally on the findings from 16 interviews with people with direct experience of the condition, patients, parents, partners and other family members and supplemented by later findings from interviews by aHUSUK. Direct quotes from interviewees are *in italic* and attributed to the category of interviewee: patient (all adults), parent, or partner/family member.

Many impacts of the condition and its treatment are similar for patients and their families, whether the patient is affected as a child or later in life. Sections 2 and 3 describe these general impacts. Section 2 reports on people's experience of obtaining a diagnosis and accessing services and information. Section 3 describes the impact of the condition and its treatment.

Sections 4 and 5 describe the specific impacts on children and adults respectively. Many of the consequences of the disease depend on the age at which people are affected. Section 6 reports on the experiences of patients who have received Eculizumab.

2. Diagnosis, access to treatment and information

2.1 Patient/ carer experiences of obtaining a diagnosis

The initial symptoms of aHUS in both children and adults are mild and similar to other minor ailments. They include headaches, sickness, diarrhoea, oedema and tiredness, symptoms also common to kidney failure. Babies become pale and distressed and stop feeding: urinary problems are sometimes indicated by '*pink nappies'*. The condition is therefore not immediately recognised by GPs and other more benign explanations are given, despite in some cases there being evidence of kidney disease in the family. Patients often report repeat visits to the doctors while symptoms persist, until the point at which their kidney failure becomes life threatening requiring hospitalisation. This happens within a very short timeframe (a few hours, days or weeks).

> *I went to the doctors about five times over Christmas and New Year and they didn't know what was wrong with me. They thought maybe glandular fever, then they said I might have got a dose of gastric flu…and eventually I got sent for some blood tests and then one morning I was really, really poorly…we phoned the doctor and he checked my blood results and at that point he was round in about 10 minutes and he told me that I'd got a problem with my kidneys and I needed to go to hospital.* ***(*Patient)**

> *Initially she was diagnosed with baby anaemia…until six weeks later when I noticed her nappies were very little and she was really bloated and I said 'This is not possible, she's not eating, how come she's putting on weight?'…I thought there must be something wrong with her kidneys… she was shiny and it looked like fluid on her legs, her legs were really big…I took her to the hospital and they took a blood sample. Then we went home and they called at nine at night to say it's HUS and she must be admitted urgently.* **(Parent)**

> *It was a case of not knowing really even though it was in my family.* ***(*Patient)**

One of the major concerns is that aHUS is not diagnosed quickly enough because it's so rare. Failure to do so mean those patients can all too quickly end up with life-threatening kidney failure:

> *I had done everything in my power – taking my son to the doctors repeatedly, taking along a sample of urine that looked like coca-cola. And the doctor didn't pick up on it at all. I'd much rather they sent hundreds of kids for a blood test to catch one or two – because that time is so precious. In 48 hours my son was in kidney failure. But if we had picked it up straight away…* ***(*Parent)**

> *I remember one Doctor said to me " We think you've got kidney failure but you are too young to have it so I think we are going to rule that one out" So I pointed out that my mum had kidney failure at 26 so it was not too young. I was transferred to HDU and put on dialysis and plasma exchange straight away.*
> **(Patient)**

Patients are immediately sent to their local hospital. Once kidney failure is detected, affected children are sent by emergency ambulance to one of the children's hospitals in the country with renal specialists. Adults are sent to the nearest renal unit. Immediate treatment is focused on restoring kidney function and treating the anaemia (See Section 3.1) although doctors are often unable to identify the underlying cause. Patients are usually tested for a range of other conditions. When these come back negative, the typical form of HUS is often suspected despite the unusual presentation, and tests carried out for a preceding gastrointestinal *E. coli.* infection.

> *They tested me to see if I was pregnant and I wasn't and they tested for HIV and I didn't have HIV…they didn't really know what was going on. They said…something like, we want it to be E-coli because we'll know what to do and it came back that they didn't know what it was, and that was the worst case scenario.* ***(*Patient)**

Parents who had lost a child with aHUS were told that their child had died from the typical form HUS. They were told it was rare and very unlikely to happen again and encouraged to have more children. It was only when subsequent children also became ill that the atypical form was diagnosed. One mother was pregnant with her third child when her second child was, like the first, affected by aHUS and an accurate diagnosis obtained. The doctors offered a termination at this point, but she refused as she was already five months pregnant. Her third child was unaffected.

Adult patients who have been given an initial diagnosis of HUS are informed that the condition is unlikely to reoccur and that their kidney function may come back. It is only when test results come back negative for *E.coli*, or the disease reoccurs or kidney function is not restored, that aHUS is diagnosed. It typically takes several months to receive a final diagnosis. One patient was diagnosed in three weeks because by chance their senior house officer had recently worked with a registrar with an interest in aHUS. Another had waited ten years between their initial illness and final confirmation of aHUS because they became ill some time before the aHUS gene was discovered. In recent years, once aHUS is suspected, genetic tests have been carried out to confirm the diagnosis and identify the individual's mutation. However the gene mutation has not been identified in all affected families, so this is not possible for everyone diagnosed with the condition (See Section 3.6).

Many interviewees reported that this experience of incorrect and delayed diagnosis had '*rocked their faith in the medical profession*' and they no longer felt the same confidence in their doctors.

2.2 Patient/ carer experiences of accessing treatment and information

Patients are usually assigned to a kidney specialist for their treatment, because often the immediate and most pressing concern is the loss of kidney function. Patients therefore receive the care they need at the initial stages. They also receive clear information about their kidney failure and sometimes an explanation of HUS. However, kidney specialists may not have sufficient understanding of aHUS to recognise, treat and explain other aspects of the condition. This becomes a greater concern over the longer term.

> *They just told me I had HUS and that was it, there was nothing else said about it .It was just "You got HUS". I did not even know it was aHUS, I didn't know anything about all that.* (**Patient)**

> *The doctors as good as they are, are not aHUS specialists. My consultant is a nephrologist and aHUS is a blood condition. Having a specialist service would stop an awful lot of anxiety because for example my son has had tummy aches for a few weeks now. They've found out that people can have small eruptions of the condition. They think these rumblings are going on in the body, which could all gather up to be an acute attack. That's what's been concerning me – are there things bubbling away in his colon? I wish I could pick up the phone and ask the doctors whether there's something that needs to be done – but I don't have the confidence that my local team know enough about the condition.* **(Parent)**

> *It beats me that when my partner goes to all these outpatient appointments at the hospital and she has regular visits by home dialysis nurses as well there is no talk about aHUS, no mention of it.* **(Partner/Carer)**

Similarly, people may be incorrectly diagnosed with other conditions which may in fact be aHUS. For example, one parent of a child with aHUS had themselves been diagnosed and treated for many years for a rare form of life-threatening asthma. Only after discovering that they themselves carried the aHUS gene, did they consider that their asthma attacks could be due to aHUS affecting their lungs. They are concerned that their chest physician will not know about the condition or its treatment and are therefore seeking referral to a specialist.

Some patients have been lucky as they happen to live close to a hospital where doctors with specialist knowledge of aHUS have been available. Others feel frustrated that their experience of diagnosis and treatment has been poor simply because of where they live. The lack of knowledge of aHUS amongst the majority of the medical profession means that patients/ families have not always received a full picture of their condition. Many interviewees reported that they only fully understood aHUS following the conference in 2011, despite having had the condition for many years.

> *There's an awful lot I've learnt going to the conference… We weren't even informed that adults could get this – we were under the impression it was only children. We were absolutely gobsmacked to see that…. For us that was massive – yet again. Nobody told us that it's life-threatening every time they have a reoccurrence. We also thought it was just in the kidneys.* ***(Parent*****)**

Many of the interviewees had initially found information for themselves using the internet. American websites were the only source of patient information until last year. Since then, the work of aHUS UK has helped to increase people's understanding of the condition. Many said they now feel they know more about aHUS than their doctors. They feel better able to recognise the symptoms. They are more proactive in monitoring and are better prepared for

repeat attacks. As they have gained in confidence, they feel able to ask for services that might not otherwise have been offered.

> *I don't think my doctors understand this condition – because when I took him in last – they checked him over – but they didn't ask for a blood test. Really I should have pushed it and said 'the only way you can tell if there is low level complement activity is by checking his blood'. I've since been on the patient website and I've printed off all the information, as it's about empowering yourself and saying to these doctors 'This is what you should be looking for.'.* **(Parent)**

Families with experience of aHUS are also better informed to ensure a more rapid diagnosis for other affected family members:

> *When some of my nieces and nephews got the test and knew they got the gene – when their children got ill, we sent them all the papers we had on it. They talked to their doctor and said 'Could it be aHUS?' The doctors looked at them as if that was impossible, they didn't know what aHUS was. (***Partner/ Family member)**

2.3 Patient/ carer experiences of accessing genetic testing

Most families in England have accessed genetic tests without any problems. However, one family reported delays in getting tested and getting the results for one of their sons living in Scotland, a similar problem was reported in Wales. One family in England experienced delays as well as receiving incomplete results because their samples were sent to a research laboratory in Paris, rather than a UK diagnostic facility. Some of the delay was caused by a local trust refusing to pay for the test.

> *It took nine months to find out who would pay for it – because our local hospital trust refused – they didn't think it was serious enough. The courier service to Paris was expensive and that's what they were quibbling paying. So my husband and I were going to have to go to a panel to say why it was so serious. That was all traumatic as well…in the end the specialist hospital paid…Our team want to have a specialist centre – which I totally agree with after the nightmare we've had, with everything taking so long and not doing the full test...* **(Parent)**

> *I have not been tested. I want to have the testing done. None of my family has been tested. My father had kidney failure (recently deceased) and my Doctor thinks it was passed down from my father's side.* **(Patient)**

2.4 Patient/ carer experiences of living with a rare condition

Many of the interviewees commented on the difficulty of the rareness of aHUS. They reported feeling lonely, isolated and '*a bit different*'. Until last year, they had not been able to access any peer support, having not been able to find anyone else in a similar position. The patient conference in 2011 was a positive experience for many. Hearing other people's stories had been informative, inspiring and reassuring. This provided the motivation and inspiration for setting up a patient support group.

> *I just thought I was the odd one out, as it were, I never really questioned it.* **(Patient)**

> *You see people going for transplant and it works.....and you are thinking you cannot have that...* **(Patient)**

3. Patient/ carer experiences of aHUS and its treatment

3.1 Patient/ carer experiences of an aHUS attack

The acute phase of aHUS is life-threatening. Two of the families who contributed to this submission had lost children with aHUS. One family had lost two babies in the 1970s. Another had lost four children in the 1980s and '90s, three as babies and one child aged six.

> *My son had had four relapses – and during the fifth one he had really bad neurological involvement and we lost him just before he was seven. It's very difficult to control once you have neurological involvement – it just seems to be completely overwhelming and then the brain can't control the heartbeat or the respiration and then there's nothing that can be done then.* **(Parent)**

During the active phase, many patients with aHUS require intensive care for weeks or months. Three of the patients who contributed to this submission (two adults and one child) had experienced heart failure and were resuscitated. This was either a consequence of the loss of kidney function or followed an allergic reaction to the treatment. Some adult patients do not have any memory of this time. Others can remember very painful experiences. Where aHUS has been triggered by pregnancy patients may experience the loss of a child or the anguish of separation from their newborn infant. This is obviously a traumatic time for partners, parents and family members. A number were told that their loved one was very unlikely to survive. They reported that they had coped by remaining positive, especially in front of the person with aHUS.

> *The whole family came running. We wouldn't have that thing where you sob by the side of them – we wouldn't let people be negative. They had to be very positive and you had to tell [the patient] what was happening…We had to keep upbeat and stay positive even when the doctors were saying 'Don't be ridiculous'. That wasn't us by nature, but that was the way we played it, because we had to find a way to cope with it.* **(Partner/ Family member)**

> *It was very traumatic because it was so full-on – my son felt so ill – we were having to rub his back, rub his stomach – distraction tactics – really full-on as well as trying not to show your emotions in front of him - so he didn't realise how ill he was – that was really difficult. When you're in hospital with children, you don't know sometimes what time of day it is – it's a very intense kind of time – very surreal.* **(Parent)**

> *It was pregnancy that brought mine on you know and I lost the baby...* **(Patient)**

> *... because I had a caesarean ,had some infection in there as well, so at that point they were more concerned about that... then I went into intensive care* **... (Patient)**

Before their illness, the patients showed no signs of ill-health. There are no warning symptoms or signs so the initial attack is unexpected – *'a bolt from the blue'*. Families are greatly shocked by this experience and their lives completely changed as a result. Many reported that this was a time they consciously tried to put behind them.

> *You're just trucking along normally – nothing bad had ever happened to us. Then it just hits you like a car crash – you go into shock. The severity of how ill [X] was in the beginning was just beyond stress. It was very, very hard. That was the bit we had to put into a box for a long time and forget about and try and not dwell on.* **(Partner/ Family member)**

We felt out of control, the control of our lives seemed to have been taken away by it. **(Patient)**

Many also reported that this trauma had contributed to heightened levels of anxiety ever since, a general feeling that '*something bad is going to happen'*. This is true for adult patients, parents and carers. At the same time, some felt that the experience had given them a different perspective on life. It had encouraged them to make the most of each day and appreciate what they have. Many said they coped with aHUS by staying focused on the positive.

3.2 Patient/ carer experience of hospital care

Once the initial acute phase is over, patients can remain severely ill for some time. Typically they remain in hospital for a further 2-20 weeks, depending on how seriously they are affected. Patients who have not suffered renal failure continue to receive plasma exchange to suppress the disease activity. Patients with renal failure start dialysis. The impact of these two treatments is discussed in Sections 3.3 and 3.4.

For parents and family members, a long stay in hospital often means '*putting their life on hold*' to provide their loved one with vital care and support. Children often need their parents to be with them full-time. Parents may therefore need to take extended leave from work and as well as ensuring that any other children are cared for. The lives of parents, grandparents, other family members and siblings are therefore severely disrupted.

My son found it very hard in the hospital. He doesn't cope with pain very well and he was in a lot of pain. He found the machines really hard work – he couldn't stand the lights and the bleeps – so both my husband and I had to be there in shifts – because my son needed to have us there. **(Parent)**

You have no life. You just live at the hospital. My husband and I took it in turns to go back and look after our son at home. All you do is come to your house, have a shower, pick up your son from school, cook for him, sleep, or work, drop him off and go to the hospital again... **(Parent)**

3.3 Patient/ carer experience of plasma exchange

Plasma exchange (PEX) is typically carried out daily in the initial stages requiring patients to remain in hospital. As patients improve, the number of exchanges is reduced, with constant monitoring to track disease activity. When the number of PEXs is reduced to 2 or 3 a week, patients can usually go home, returning to hospital for their treatments. Although the treatment only lasts 2-3 hours, these visits usually take much longer with the travel time, waiting times, blood tests and recovery time. Parents/ carers need to attend these sessions with their children, which is disruptive to daily life and the wider family. Parents reported that their children appeared to cope well with the PEX treatment.

Some patients can be gradually weaned off PEX and go into remission. Others may be more severely affected and find they are unable to reduce the number of treatments to below 2 or 3 times a week without a reoccurrence. The treatment needs to continue all the time the disease is active. For example one child with aHUS had received PEX three times a week for over three years, with repeated reoccurrences, before being given Eculizumab in 2011 (see Section 6.1).

PEX is carried out via an implanted catheter or 'line' in a vein. Patients require an operation to place the line and this is difficult to do in babies and young children. Lines need to be protected from infection, which prevent patients from having a bath or swimming. Large, very sticky, waterproof dressings are used, but infections are not uncommon. These can be

serious and life-threatening, especially for young children. Infected lines may need to be taken out and replaced. During this time, while infections are being treated, the patient is no longer receiving treatment and the aHUS can reoccur, requiring hospitalisation. There is a limit to how many times lines can be replaced.

> *The body only has so many ports – places where they can put lines and we were warned that she would run out of ports eventually... That was a major concern – because you have to keep at least two ports available for a future transplant and she was running out of ports.* **(Parent)**

Lines can also come out causing great distress to all involved.

> *I was taking my son to school in the morning as always, I was on the driveway, and the lady who was helping us at the time, she came running up and said the blood is coming from everywhere and basically my daughter's line had fallen out, because of the pressure there was blood everywhere…***(Parent)**

Adult patients reported that the treatment itself can be difficult to tolerate as there are many side-effects (see Section 6.1).

> *...After fourteen years it does take its toll, it is bound to take its toll on your body ...* **(Patient)**

3.4 Patient/ carer experience of dialysis

Dialysis may be required temporarily if kidney function is lost during the acute stages of aHUS. If a patient's kidneys are permanently damaged during this phase, they will need dialysis for the rest of their lives. People with aHUS may not have the option for a transplant (see Section 3.5).

> *You have kidney failure and that's really what living with aHUS is for me, it's living with kidney failure. I don't live with aHUS, because I only got it twice, when it first happened and when it came back in the transplant - those are the only two episodes that I've ever experienced.* **(Patient)**

In the short term, haemodialysis is carried out through a central line either in the neck or groin. This is uncomfortable and liable to infection. Peritoneal dialysis is often the first choice for long term dialysis as patients can return home quickly. However it is difficult to manage, often not as effective as haemodialysis and is associated with serious side-effects. Two of the patients who contributed to this submission had developed encapsulating sclerosing peritonitis (infection and scarring in the abdomen that interferes with bowel function and prohibits further peritoneal dialysis). Many patients therefore switch to long-term haemodialysis.

> *I had opted to try a system of dialysis at home which involved an exchange of fluids through a catheter in my peritoneum. It frequently went wrong. I hated every minute and every aspect of it. It required a lot of equipment, training, and had to be done 4 times a day taking about half an hour. It did not make me feel better, I was permanently anaemic, exhausted and frequently ringing my husband who was trying to work, to take me to hospital to sort the catheter out. My days consisted of lying on the settee too weak to do anything, unable to eat due to 2 litres of fluid in my abdomen causing discomfort - quality of life nil.* **(Patient)**

3.4.1 Preparation for long-term haemodialysis

For long term haemodialysis a site for vascular access needs to be prepared, which is the site where blood is removed from and returned to the body. The best way to do this is with a fistula, which requires surgery and involves connecting an artery directly to a vein, most often in the forearm. Sometimes veins are removed from the leg and grafted to the arm. The fistula causes more blood to flow into the vein. As a result, the vein grows larger and stronger, making repeated needle insertions easier. It can take weeks or months for a fistula to be ready for use.

Fistulas need to be carefully maintained, placing some restrictions on the patient's life. Patients are advised not to carry anything heavy or to have blood taken from that arm. The fistula is unsightly which affects what people wear and makes them feel self conscious (See Section 5.2). Fistulas need regular checking to ensure they do not become infected or blocked by a blood clot. Treatment is required if this happens. Some may need stretching with angioplasty which is painful. Keeping their fistula clear can be a source of constant anxiety and concern for patients on dialysis, especially when previous grafts or fistulas have failed.

> *At the end of the day I'm being kept alive through this access to dialyse, and if that access goes, then that's that. So they [the doctors] are really fighting to keep this lifeline, but I don't know how much longer I'm going to be able to keep it…* **(Patient)**

If patients choose to dialyse at home, parents, carers and adult patients need a month's training in managing the process, learning how to put the needles in, how to set up the machine and how to cope with any emergencies such as blood clots, infections, a blown vein (pushing the needle through the wall of a vein leading to painful blood loss into surrounding tissue) and air bubbles in the line which can be fatal.

3.4.2 Managing dialysis day-to-day

For aHUS patients with kidney failure, it's dialysis that has the biggest impact on their day-to-day life. They have no option but to dialyse 3-5 times a week, which severely restricts their freedom. Every day is scheduled around dialysis. Children's freedom is restricted in simple ways, for example not being able to stay over with friends.

> *The main thing about dialysis is the lack of freedom, and the things that people take for granted…Trying to plan things is a nightmare because I don't know how I'll be feeling. I don't know where I will be in 2 weeks' time because I could change things around or swap things over. You can't ever be spontaneous…* **(Patient)**

There is some variation in how much individuals need to dialyse. There are different kinds of dialysis and choices about whether to dialyse at home or at hospital. Going to hospital is more restrictive as patients are given a time slot (e.g. 5pm on a Monday, Wednesday and Friday) that they cannot change. Several patients are given the same time slot, and all have to wait their turn to be connected to a machine by a nurse, causing delays. Some people prefer this option as they are able to clearly separate dialysis from the rest of their lives.

Some patients/ parents choose to dialyse at home. This gives them some flexibility and control over their time. Although patients can never miss a session, they can be flexible over the timing of their sessions within a 24 – 48 hour window. This makes it considerably easier to manage day to day life. For example, one mother described how she timed her daily sessions so as to be able to drop off and pick up her daughter from nursery. However, managing the process takes a considerable amount of organisation and planning.

Having dialysis at home can feel invasive. Therefore if they have the space, patients/ families tend to set up a dialysis room, to keep it separate from the rest of their home life. However, there is still a large volume of equipment required in addition to the dialysis machine, for example paper towels, new lines, artificial kidneys that are delivered regularly and need to be stored '*all round the house'*.

Dialysis is extremely time-consuming. One of the adult patients who has dialysis during the day, five times a week estimated it takes 35-40 hours a week. Some patients have chosen to dialyse overnight, which minimises the impact on daily life. For parents, managing their child's dialysis and working, leaves very little time for anything else.

> *I come in from work about 6 - 7 and the first thing I have to do is set up the machine, I finish that by 8… then you obviously have to connect her. So this is it. This is my evening… For me it's a constant, constant rush. It's just a daily struggle to cope with everything. And it's the other things like deliveries, and you have to order the medicine, and cleaning, and check-ups. (***Parent)**
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> *...It is like another job to me and I am going to do my job. (***Patient)**
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> *I think of it as like spring cleaning, something you don't like to do but you have got to do it and that is the way I look at it.* **(Patient)**

The process is also demanding, as it requires technical skill and careful management to avoid infection. The entire process from start to finish involves:

- Heating the machine to disinfect it
- Washing patients and carer's hands – for two minutes with harsh, antibacterial soap
- Setting up a syringe that drives an anti-clotting agent into the blood throughout the dialysis
- Priming the lines with saline to prevent air bubbles getting in
- Calculating how much fluid needs to be removed – based on the patient's current weight and past dry weight (immediately after the last session). This is programmed into the machine. As much as 3.5 litres can be removed at any one time, but removing this much fluid leaves patients drained and exhausted, which is why they restrict their fluid in between dialysis sessions
- A blood pressure check.
- Two large (1.6 mm) needles are then inserted into the fistula and the dialysis begins – 400 ml of blood goes into the machine – this blood loss can cause blood pressure to drop and make the patient feel ill.
- While on dialysis constant checks are made to ensure the machine is working properly, there are no leaks in the lines, the needles are positioned properly etc.
- Being on the machine is draining and there can be serious side-effects – painful muscle cramps, migraines and a fall in blood pressure – which can make the patient feel extremely ill.
- At the end of the dialysis, the blood in the machine is washed back into the body using saline. The needles are removed. The blood in the fistula is under the same pressure as an artery, so the site needs to be taped/ pressed on for 10 minutes to prevent blood loss.
- The machine is cleaned and the room cleaned and sterilised.

The entire process takes 4-5 hours. It is not relaxing. Patients often need to sleep for a couple of hours afterwards to recover.

> *Whilst on the machine you feel progressively drained and your anxiety to come off increases… I also get very itchy all over my body…. It is hard enough that you are*

trapped on the machine, but you also feel uncomfortable whilst you wait. Clock watching is a common past time… **(Patient)**

The common frustrations of modern life take on a greater significance for dialysis patients.

If there's a technical fault, you can't go on dialysis until a technician can fix the machine. Technicians don't work on Sundays or after 4.30pm. Another complication is when the water pressure drops or there is a power cut. When people were talking about the petrol strike, I was worrying about how I was going to get to my dialysis… **(Patient)**

Patients cannot dialyse alone. A parent or adult carer needs to be on hand at all times in case something goes wrong. The machines are fitted with an alarm. A number of parents/ carers reported that they feel quite anxious during dialysis, constantly listening out for the alarm. During overnight dialysis for their children, some parents report they have a much poorer night's sleep. One parent described how she had once slept through the alarm when her daughter's line had become clogged with a blood clot. She was able to take her daughter to hospital to have the problem resolved, but she lost her confidence. She now chooses to put her daughter on dialysis late in the evening through to one or two o'clock in the morning, even though she has to go to work the next day, because she knows she can stay awake during this time. Being a parent or carer for someone on dialysis can therefore feel like a huge responsibility. Many interviewees said it feels '*unrelenting*' as there is no option to stop or take a break, no matter how ill the patient or the carer may be feeling.

If I had severe diarrhoea, severe sickness and I was crawling on that floor I would still have to go to dialysis…Two weeks ago I had a really severe chest infection and I had to be taken there in a wheelchair. I didn't feel like going but you have to… (**Patient)**

3.4.3 Impact on quality of life

Patients do not always feel well on dialysis. Children are often tired and sick because of the shifts in fluid. Adults report sleepless nights, cramps, headaches and migraines. This is because dialysis is a poor substitute for a functioning kidney. Other aspects of kidney function are compensated by other treatments e.g. injections of the hormone erythropoietin to regulate red blood cell production, but these treatments are also not as effective at maintaining the body's balance. Dialysis patients therefore experience see-saw side-effects of high or low blood pressure, overly high levels of haemoglobin or anaemia.

Dialysis patients and their families are able to go on holiday, but only with considerable planning and organisation. It is not a simple choice. Some patients are too fearful of the risks. Others reported that it took five years for them to build up the confidence to do it. Parents have taken their child's dialysis machine with them. Adult patients are able to book dialysis sessions at the local hospital at their holiday destination, abroad and in the UK, although availability may be limited. This restricts families' choice about where they go on holiday and for the person with aHUS, much of their holiday time is spent in hospital.

You just wouldn't believe what we had to take on holiday, how long we had to spend arranging everything…It is possible, and I wanted to go for holidays like everyone else…I think we started to arrange it more than half a year ago. The fluids had to be delivered, we had to take the machine…We had to arrange a hospital over there so that if anything was to happen, we could go there…And for me particularly it's not a holiday because we still have to do the dialysis. **(Parent)**

3.5 Patient/ carer experience of kidney transplants

Patients with aHUS are not always recommended to have a transplant because of the likelihood of the new kidney being damaged by the disease. Amongst the aHUS affected patients in the UK, 16% have had a successful transplant (personal communication – Professor Tim Goodship). Six of the adult patients who contributed to this submission had undergone this procedure. In two cases, the patients felt the doctors had not sufficiently explained that the aHUS might come back and had every hope of the transplant working. In the four other cases, the patients and families were aware that there was a reduced chance of success, but there seemed to be no other option. None were successful. Patients had their new kidneys removed within a matter of weeks. The physical and emotional impacts were severe for the patients as well as for parents or partners who had been donors. This was a topic interviewees felt unable to talk about.

> *Well they left me in the room with people whose [transplants] are working. Well they were being so happy; I think that is what got to me in the end. I never talk about anything to do with transplant, I never talk about it.* **(Patient)**

> *...and I have seen people coming back and it would be working and they are happy and then they tell you your kidney was failing and you've gone through all that for nothing.*(**Patient)**

3.6 Patient/ carer experience of living with a genetic condition

In some families, there is no history of aHUS, prior to a single family member becoming ill. Others are able to trace the disease back through 2 or 3 generations and have several family members affected at the same time. Therefore parents (and other family members) often only become aware of their own risks, once their child or sibling has been affected. Once discovered, this leads to increased anxiety about their own health as well as concerns for others. Many reported managing this anxiety by trying not dwell on their fears.

> *Knowing that I've got the gene, I've sort of put it to the back of my mind. My philosophy always has been that you live life. Recently I've been thinking what about the rest of the family that have got the gene, but there's nothing you can do. You can't think about it all the time.* **(Partner/ Family member)**

> *My worry then is, if it's been passed down, about my nephews and nieces, I worry about them.* **(Patient)**

Parents with an affected child often choose to have genetic tests themselves either to allay concerns about their health or because they have been tested as potential donors. Once identified, the affected parent then faces the challenges of informing the wider family, their own siblings and nieces and nephews. Some people want to know about their genetic risks to inform their life choices. Others say they would prefer not to know their status to avoid the anxiety, particularly as not everyone with the aHUS gene mutation develops the condition and there are no measures to prevent the disease occurring. Decisions about who to tell and what to tell them, can place considerable strain on individuals and family relationships.

Parents also face difficult choices about whether to have all their children tested once one child is known to be affected. Some choose not to have their children tested so as to reserve their children's rights to find out for themselves. Others find they become so anxious whenever their children become ill, that they feel them simply '*need to know*'.

Some families do not have this choice, because although a family member has been diagnosed with aHUS, doctors have been unable to find their particular genetic mutation. This means they cannot look for it in others. These families therefore continue to live with the uncertainty as to who might be affected. This occurs in about 10% of cases.

*People say to me, 'It won't be long before you have grandchildren' and I think 'Oh no'. All that worry again – it's just going to be horrendous. And other people in our family of the same generation as my children are now having children – which is a worry as we don't know where it's come from. For now everybody just pushes it to the back of their minds. But it's something that never goes away. (***Parent)**

3.7 Patient / carer's overall experience of living with the condition

There are many sources of stress and anxiety with aHUS. After the initial trauma of a life-threatening episode, patients and their families live with the constant threat of a reoccurrence. Each reoccurrence is likely to lead to further kidney damage and eventually renal failure, or could potentially be fatal. Some patients report that their emotional well-being is much affected by a fear of dying and knowing they have a reduced life expectancy.

There are currently no markers to indicate whether a reoccurrence will happen, when it might happen or how serious it might be. This means families have to live with a great deal of uncertainty. Patients with other reoccurring conditions with severe relapses, for example multiple sclerosis, find this uncertainty to be one of the most difficult aspects of the condition to live with[1].

It's this constant worry, constant stress that you don't know what will happen. The unpredictability is just killing. **(Parent)**

My son's first episode was so traumatising – and then to find out that you might have to go through that again… It's that million-dollar question - will he be one of those lucky people who never get it again? It has been a lot for me and my husband to get our heads round – so how do you tell a child about that? I don't think he needs to carry that on his shoulders yet. If he asks about it I'll tell him, but I'll be fairly blasé about it until I feel he's ready to take it on board. **(Parent)**

Parents with children with aHUS in remission, (as well as those who know their unaffected child carries the gene) report having to manage their anxiety every time their child becomes ill, because the start of aHUS looks like many other common childhood illnesses. However all concerned, including family GPs, now feel more confident about recognising the signs of aHUS so that if there were a next time, their child would be treated more quickly.

We try not to over worry or otherwise every time she got a runny nose we'd take her down the doctors, so we try not to do that – if she's got a cold we keep an eye on how often she's going to toilet – it's always on the back of your mind. **(Partner/ Family member)**

Those patients who have reached end stage renal failure report that '*aHUS has done its worst*'. However, they and their families have to manage the daily stresses of life with dialysis (See Section 3.4).

Many parents, partners and carers of people with aHUS reported that living with the condition had taken a toll on their mental and physical health. These problems included high blood pressure, anxiety and panic attacks. Some were receiving medication to manage these problems. Others were receiving counselling. One parent thought counselling should be offered routinely for families with aHUS. This is not often the case.

[1] Living with the effects of MS. The MS Society. www.mssociety.org.uk

> ***...****I do not go out anymore you know I am frightened something else is going to go wrong...***(Patient)**

All of the interviewees talked about how they had learnt to live with the demands of the condition and its treatment and to some extent had forgotten what it was like to live a 'normal life'. It's only when looking back or talking to other people that they wonder how they have managed.

> *The questions you would expect, like, why me, why now, they sort of disappeared, because you get used to this life and you think that it's been like this forever, and it's almost forgotten that it can be different.* **(Parent)**

4. aHUS in babies and children

Children were not interviewed for this submission, because all of the children involved (except for one) were under the age five. The oldest child is not aware they have aHUS. Therefore this section is based on the reports of parents and other adult family members.

4.1 Impact on the child's well-being

Most babies and young children appear to cope extremely well with their early experiences of their condition. (See Sections 3.1 - 3.3).

> *My daughter was obviously very young when she was diagnosed which I'm grateful for – as she hasn't known anything different. She's quite comfortable in hospital and looks forward to it – which sounds crazy – but the hospital staff are almost friends to her.* **(Parent)**

One part of the treatment which is particularly difficult for children is the large numbers of blood tests required and the repeated access to veins for infusions.

> *They had to take him into theatre and give him an anaesthetic to get to a vein because he was still under two. But he was reacting very badly to the anaesthetic every time. Normally he's a placid child, but he would scream for an hour or two after the anaesthetic.* (**Partner/ Family member)**

Some children need to be held down initially, but over time they become more used to the procedures involved. Other children develop hospital or needle phobias after the trauma of the initial aHUS episode.

> *It's had an impact on my son's mental health. Being in a hospital or at the doctors – he's very anxious – he can be under the table – sometimes he never even makes it into the room. We've learnt over time how to manage it and calm him. He hates needles – when he has blood taken, we've had to have 4 or 5 of us hold him down. Last time he had gas and air and he thought it was great – so now we've got something that will reduce his anxiety.* **Parent**

The ongoing impact of aHUS depends on which organs have been affected. Children with kidney failure face the similar challenges to adults in managing the restrictions of dialysis (See Section 3.3). Some children also experience brain damage during an initial aHUS attack with consequences for their daily life and ongoing care.

> *My son later had problems with his balance. It didn't manifest itself until about 15 months when he was having difficulty walking. Then he was having a lot of*

physiotherapy and we got quite involved in conductive education because he had ataxia. So he had a lot of input from other services and he couldn't go to a normal school. **(Parent)**

4.2 Impact on daily life

Children with aHUS who have lost their kidney function often do not eat because they lose their appetite. They are therefore fed through a nasal gastric tube or directly into their stomach. The latter is better for children at school as the tube can be kept out of sight and the children themselves find it easier to cope with. One of the children included in this submission is supported at school by a teaching assistant who has been trained by the hospital to feed her twice a day and to monitor her fluid uptake. School staff are often very supportive and heavily involved in managing the condition.

4.3 Impact on schooling / education

Children with aHUS who continue to receive treatment inevitably miss time at school. Not only do they miss the days they are having treatment, but every time there is a problem, e.g. an infection, they may miss weeks of school while in hospital. Parents and teachers cannot always compensate for the loss of time.

Initially the first year it happened she wasn't basically present at school, now later on, at least once a month we have to go to clinic, then there's all the other extras on top of that…when I speak to the teachers, they say she's making good progress but she's always in a lower group, and I think she's a bright girl, but she missed a lot, and I cannot give her that time at home, to make her catch up, because we struggle with time so badly [with dialysis]. I think I would need to quit my job to take care of that problem. **(Parent)**

4.4 Impact on parents' well-being

In addition to the long term stress and anxiety (see Section 2.7); some parents also develop a 'fear' of hospitals.

For the last four years I'm just like a robot, but still I do everything to stay out of hospital. I'll do anything because I had such bad experiences…In the hospital every single child has a very serious disease…So if you are around that all the time you're just going down… **(Parent)**

4.5 Impact on parents' work and ability to earn a living

Parents whose child requires continuous care, e.g. regular plasma exchanges in hospital (See Section 3.3), may have no option but to stop work. Others report that they are fortunate in being able to fit their work flexibly around their child's treatment. Nursery or childcare may not be an option. Other family members are relied upon to provide more specialised childcare as they will have been trained in managing the condition. Grandparents, who are retired, often provide a lot of childcare. In addition, grandparents and other family members sometimes provide financial support.

4.6 Impact on siblings/ other family members

The brothers and sisters of children with aHUS are often affected by being left in the care of others, while their parents spend long periods in hospital with their sibling.

The other child doesn't see their Mum and Dad as often as they'd like. It's not good for children to be separated from their family. I don't think my granddaughter could understand why she was with grandma for what seemed like weeks on end. We took

her up to see her brother when we could – but Mummy and Daddy were away a lot of the time. You try to make life pleasant for them but it's quite a strain on grandparents too. **(Partner/ Family member)**

Parents report that they find it difficult to give their other children sufficient attention.

My son's life was very limited because our life was, unless friends offered to take him somewhere, we couldn't...It was very difficult. Even a trip to the cinema, you're there, but you're not there, you're thinking what if I have to go back, what if something happens… and he became part of it, and he's like 'It's time to do blood pressure, let's go and hook her on the machine'... and at the same time I have to say to him 'Don't come into the room, because you've got a cold, you didn't wash your hands'... ***(*Parent)**

Some siblings cope extremely well. Others had exhibited behavioural problems, most likely resulting from the stress and lack of attention.

When you are constantly involved with one child, it's obvious that you don't have much time for the other one and he's been affected by that…he's got these aggressive outbursts… it's kind of he wants attention basically, but everyone in the household is really emotionally exhausted. It's been four long years. No one has any more patience in this house. **(Parent)**

4.7 Impact on relationships

Having a child with aHUS places considerable strain on relationships. A number of parents are no longer together. However, some parents say the experience has made them closer, and that they work well as a team supporting their child.

5. Impact on adults

There are two peak ages where adults develop aHUS, in their early 20s and in their 60s. The impact of the condition on people's lives is very different at these two life stages. These are highlighted in this section.

5.1 The impact of the condition on life events

In their early twenties, young adults are just about to embark on their lives and make choices about relationships, careers, where they want to live, buying houses and whether to start a family. Developing aHUS at this age therefore has an impact on all these life decisions.

*It's like one of those pivotal moments in your life. I don't think I'd be living in here, I don't think I'd be living in Britain if I hadn't got kidney failure…I was ready to leave home and do my thing and it just stopped me in my tracks really***.(Patient)**

After the initial attack, some people never become well enough to return to work. Some have managed to do so, but have taken 2-5 years to recover their health to the extent that they could go back to work or resume their lives, for example to return to university to finish a degree. They relied on their parents for a lot of care at this time (See also Section 5.5). They report the sense of having lost a significant chunk of their lives to the disease.

I had to go back living with my mother, and I couldn't afford my own place any more. **(Patient**)

Women of child-bearing age with aHUS (or with a genetic risk of aHUS) are advised not to have children, because pregnancy is thought to be a trigger for the condition. Young women with kidney failure are also warned that it is not possible to carry a pregnancy to full-term on dialysis, and that their babies are likely to be still born or severely disabled. Young women with aHUS have therefore often made the difficult decision not to have children. Couples have also been turned down for adoption because of one partner's kidney condition.

> ...*I lost the baby then but I wouldn't try again, you know thinking "are they going to have it?"* **(Patient)**

Developing aHUS at a later age clearly doesn't have these same impacts. However patients report that their life-long plans for retirement have been stalled or prevented by aHUS.

5.2 Impact on adult patients' well-being

Following the initial acute phase, patients report experiencing depression, loss of confidence, self-esteem as well as problems with anxiety and nightmares.

> *I suffered panic attacks quite a lot which was brought on by the dialysis and when you're first on dialysis your heart starts to beat a bit faster anyway… and the reaction to that and the stress and the panic…***(Patient)**

Patients report that their emotional health improves to some extent over time, particularly with support from families and counselling. Parents and siblings have often provided the necessary motivation and encouragement to enable patients to make the effort to get stronger and resume their lives.

People on dialysis report that the treatment itself also affects their emotional well-being:

> *I've got memory loss and depression because the kidneys don't just filter. I get aggressive when I need dialysis because of the toxin build-up and I get really upset when I can't get my needles in…I do cry and I feel like I could smash the house up – I don't obviously. Once I've done it I'm fine.* **(Patient)**

> **...***it has affected her health, well being, attitude, it is sad to see, I mean when she's on top form... but she is not on top form often enough. It is really getting to her now...* **(Partner)**

Some patients can also feel self-conscious about their scars, which can be large and considerable in number. After years of aHUS, patients have scars from their lines, fistulas, vein grafts, kidney removal/ transplants and catheters. Young women have experienced loss of self-esteem from the scarring, but report finding it easier to cope with as they grow older. They still tend to keep their scars covered. Some report feeling judged by other people.

> *People see my arm and see my fistula and think I'm a drug addict. People pull their kids away from me. That's not their fault because they don't know about it.* **(Patient)**

5.3 Impact on daily life

Adult patients on dialysis are severely restricted in their diet and daily fluid intake. They are advised to limit their daily fluid consumption to 500-1000 ml per day, which also includes any fluid in food, e.g. gravy, yoghurt. They need to maintain a low-potassium diet because if their blood potassium levels become too high they are at risk of a heart attack. Potassium-rich foods include all fruit and vegetables and chocolate. Any vegetables need to be boiled twice to remove the potassium. Patients also need to limit their phosphate intake as this can lead to calcification of the arteries. Dairy products are therefore restricted because of their phosphate levels. Salty foods are avoided as they make people thirsty. Some people avoid alcohol as it reduces their will-power to stick with their regime. People find this diet difficult to manage.

> *I want to eat the whole bar of chocolate, and I pretend I don't want to, but actually I can't, and it's just so restricting, ridiculously restricting. Every time I eat anything I always calculate the potassium content, the phosphate content so that I can think for the 48 hours that I'm not on the machine what could I get away with, how sneaky can I be, and how much can I get away with.* **(Patient)**

> *It's a big balancing act with everything. We have to keep a balance on my wife's diet – if she has too much of something she can feel tired and dizzy – but there's no blood testing kit you can have at home, like there is for people with diabetes. If you take your bloods off to hospital you can have the reading in five minutes – but there's nothing like that for renal patients. So that's always a constant worry whether something is going to be too high or too low.* **(Partner/ Family member)**

> *I think getting up and going and doing whatever you like without having to think "Oh god I've got to get back for dialysis" that would be the best ,the best way to live your life...* **(Patient)**

These restrictions inevitably affect other family members when shopping for food and cooking family meals. Meals may have to be prepared separately for unaffected family members, so that they get the nutrition they need. However, family members can feel uncomfortable about eating and drinking in front of the person with aHUS as it seems '*unfair and marking them out as different*'.

Patients/ families find it difficult to eat out as there may only be one choice on a menu available to them. There maybe nothing they can eat on special occasions which often centre on eating and drinking.

> *I went to a wedding and I didn't eat at the wedding and with all those situations, I hate the fact that I have to be so controlling, it's not in my nature to be so, I'd like to be more laid back about things…* **(Patient)**

5.4 Impact on patient's ability to work and earn a living

Some aHUS patients of working age are well enough to continue work and manage their dialysis. However, trying to manage a job and regular daytime dialysis leaves very little time for anything else and patients have found it unsustainable. They have reported becoming more ill as a result and have had to stop work temporarily or permanently to recover. Some people with aHUS have therefore chosen to dialyse overnight to give them more free time in the day. However, as one patient described, she still does not have the physical energy or emotional resources to cope with a full-time job. She therefore works part-time which is a source of some frustration, because she feels discriminated against in terms of her pay and access to promotion.

I worked all my life and when I had this kidney failure first of all I had to give up work. **(Patient)**

Other patients have reluctantly chosen to take early retirement as they have become too ill to continue working.

I was in my job for twelve years and I loved it. My bosses and colleagues were really supportive, even when I needed to take time off. But they kept saying to me 'When will you take ill-health retirement? You do need to'. I put it off and put it off, until my consultant said you really need to increase your dialysis. You won't live past 40 if you don't. Three days a week isn't enough for you. So now I dialyse at home five days a week and I'm loads better. **(Patient)**

Some families have found themselves in serious financial difficulties, having to rely on a single wage-earner and maybe forced to make unwelcome changes such as moving house or selling their car. Some receive benefits. Home haemodialysis patients are entitled to disability living allowance. This can go some way to helping with the additional costs. Some of the main costs are parking and travel for regular hospital visits, estimated by one patient to be between 50-100 visits a year. People who have stopped work through ill-health are also entitled to employment support allowance. However, proving eligibility for this benefit, managing the continual changes in allowance levels, and the knock-on consequences for other entitlements is '*hard work'* and another source of stress. Some people find it difficult to be on benefits.

The aHUS it takes away your self-respect in a way, because I've always been brought up, you have to work for what you earn… I went to college, I did my nursery nursing, and then all of sudden to go on DLA, I hated it… **(Patient)**

Now it's a financial struggle to be honest –if I could work tomorrow I would. **(Patient)**

I have worked all my life and when I got this kidney failure first of all I had *togive up work**(Patient)***

*...it took me four years to get disability [allowance} because they would not give it to me..(**Patient)***

5.4 Impact on quality of life

All the adult patients reported having adapted their lives to be able to manage the treatment for this condition in ways that have surprised them. For example, one young woman described how she would have never believed she was capable of putting her own needles in, but now does that five times a week. This is largely because people have no choice but to dialyse, and therefore have to manage its stresses and complications. They feel this is an unacceptable quality of life, but it is one they have to accept.

I see a lot of blood. I see a lot of blood clots. The other day on the machine, I forgot to put a clamp on and the blood poured out of the machine, so my blood was in a pool on the floor. It's 6 o'clock in the morning so I'm shouting to my mum to come and help me because she hates the alarm. Something had gone wrong with the machine and I was having to pump blood back into myself… and me and my mum were just laughing, she was like mopping up blood off the floor and I was like 'When did this stop being shocking to us…anyone else would be shocked…' **(Patient)**

I would not needle myself I was like "ooooh" and they had to chase me to needle me because I was petrified ...I was petrified! But now it's a job to me and now I have to do my job. **(Patient)**

5.5 Impact on social life / relationships

Adults with aHUS say the condition affects all their relationships. Young people embarking on new relationships, worry about when to tell new partners about their condition and how they will react. Many early relationships end for this reason, because other people feel unable to cope or manage their fear. This obviously impacts on the patient's self-esteem and emotional well-being.

When you meet new people or start going out with someone it's really hard. For the first date I pretended to go to the toilet. I don't go to the toilet, how weird is that? But I pretended to go to the toilet so I would look like a normal person… **(Patient)**

All family relationships are altered if young adults are forced to become dependent on their parents again. Family dynamics can change, as the affected person takes prime position in the family, even if they may not want to, and everyone around them feels they have no choice about it. Children may not receive the attention they need when their parent becomes ill.

My youngest son was a teenager when my health first started to deteriorate .Consequently, he was really rather neglected at a difficult time in his life. Neither of us was able to support him and normal family life was crumbling around him. His education suffered, he gave up A levels, changed direction several times, went from job to job. When he had started high school he had had a bright future. **(Patient)**

Families supporting a person on dialysis can end up spending a lot more time together than they might otherwise do, and not really because they choose to. Partners, parents and siblings tend to share the responsibility of supporting the patient during dialysis, as the main carer may not always be well enough or may need a break. On the positive side, this experience tends to bring families closer together.

Most people with aHUS report that their friends are understanding and supportive and will organise social events so as to make it easier for them, for example, ensuring that '*nights out won't all revolve around eating and drinking'*. Some people feel their social lives are affected, because they aren't invited out as often, because friends assume they won't be well enough or for example, that they won't be able to stay over for a weekend.

5.6. Impact on partners/ carers

As well as the high levels of stress and anxiety associated with this condition (see Section 2.7), partners and carers also have to manage the restrictions on their own lives. Their social life and other interests/ hobbies may be limited by dialysis and the unpredictability of the condition. Some partners/ carers have given up work or gone part-time to be able to provide care, which again has financial implications for the family.

Doing dialysis at home you're never in a routine – you never know what's going to happen or how well she'll feel after a session – then we can't do stuff as a family... Or we have to cancel things at the last minute. Then people stop inviting you and asking you to go out. It's had a knock-on effect with my mates asking me to go out to the pub…we try to do our best to juggle and keep all of us happy at the same time. **(Partner/ Family member)**

Partners/ carers may have to take on more responsibility in the management of day-to-day life than they might do otherwise, which affects their own well-being.

> *My husband can get a bit down because when I'm well I try to do things like gardening or decorating – and he'll say "rest, rest, rest" because you'll make yourself bad the next day, which I do. But when I'm well I want to make the most of it, I hate not doing something, I hate just sitting – it's not me. I think he takes on stuff sometimes that is too much, just so I won't do it…* **(Patient)**

Partners can find themselves, more often in the role of carer, than as husband or wife. Dialysis can also restrict their physical relationship.

5.7 Impact on siblings/ other family members

Other siblings/ family members report that their lives have changed dramatically as a result of having a person with aHUS in the family. Their life choices, for example about where to live and their jobs, can be restricted by needing to be close to their family. This is ongoing and affects their own families too, for example their husband/ wife may not be able to take a job promotion if it means moving house. To some extent this is a choice individuals make for themselves, but at the same time, they can feel a responsibility to others, to provide support to the whole family and do their share of the caring e.g. in managing dialysis.

Some family members who take genetic tests and find they are unaffected, report feelings of guilt, particularly when this means they can make life choices that are not open to the person with aHUS.

> *The impact was massive on the family – it has affected us all and changed the course of all our lives. It still does. Every day. It's so engrained in us now – you're not always aware of what impact it's had. It's only when you talk to other people and they react. You can't think about it – it would just eat you up.* **(Partner/ Family member)**

6. Patient /carer experience/ expectations of Eculizumab

6.1 The impact of the new drug on patients with aHUS

The impact of Eculizumab depends on how seriously people are affected by the condition and the stage of life at which they are affected. It can eliminate the need for time-consuming and invasive treatments. It can help patients retain whatever kidney function they have retained since having aHUS and in some cases can improve kidney function. For patients with kidney failure it offers the opportunity for a transplant and a better quality of life.

The different impacts of Eculizumab on the lives two children with aHUS and an adult patient are described in the following case studies.

Child A

Child A first became ill with aHUS at the age of 4 months. She spent 3 weeks in intensive care and remained in hospital for a further five months. She received plasma exchange during this time. She returned home, but was unable to reduce the frequency of treatment without the disease reoccurring and therefore continued to go to hospital three times a week for treatment, for the next three years. She also had regular line infections and repeated relapses which required hospitalisation. Her mother stopped working to provide the necessary care. As with many young kidney patients, she stopped eating at around age 2 and had a gastric tube fitted into her stomach. At the age of 3 she lost her kidney function due to the relapses and started dialysis. Her parents began discussions with the doctors

about the possibility of a combined liver and kidney transplant. This was a very bleak time for the family.

The following year aged 4 she was given Eculizumab. She has been receiving the drug for nearly 12 months. During this time, she was admitted to hospital on one occasion for a planned operation to have her non-functioning kidneys removed. She no longer needs plasma exchange, but continues overnight dialysis. She has had no further relapses. She has been placed on the transplant list for a new kidney.

Her parents describe the impact:

> *She became a lot less lethargic – even her nursery said she was coping with everything a lot better – she was more active and interested in things – like a different child. The main impact for us is that she's been able to go to school with children of her own age. We were thinking she might not be able to go to school. She's a lot better socially because of school. She's very sociable and enjoys life very much… The drug has also opened up the possibility of a transplant and a return to normal life for all of us.*

Child B

Child B started to become ill at around 6 months and was admitted to hospital with kidney failure at age 7 months. She was in hospital for two months and received plasma exchange. Her kidney function did not fully recover. She returned home where she continued with overnight peritoneal dialysis and hospital visits three times a week for plasma exchange. She was also receiving a blood transfusion every two weeks which was a cause for concern as it may have affected the success of any future transplants. She was on a strict diet and limited fluid intake.

She was then given Eculizumab at age 1½ and stopped the plasma exchange. Within two weeks her kidney function was restored as her mother described:

> *We were still really strict on how much fluid she was taking and weighing every single nappy to see if everything was OK. She was drinking around 600mls then a day and she was weeing everything out. You couldn't believe it - how well it worked and how quickly.*

Child B was then able to stop the overnight dialysis and had her lines removed. She has been receiving the drug for a little over a year. She goes to hospital every two weeks for an infusion. This is given through a canula, which is distressing for her. She has to be held down while the canula is fitted. She does not appear to experience any side-effects, other than headaches the first few times and a bit of dizziness during the infusion. She lies down during the treatment which lasts about an hour, remains under observation for an hour and then '*she's fine and walks away'*.

She has had a few common childhood illnesses during this time, colds and flu. She caught a stomach bug and returned to hospital because she was dehydrated and needed a drip. Everyone was concerned this would trigger a relapse, but she had no problems and her blood test results have all been fine.

Her mother describes the impact of the treatment:

She is thriving again. She started eating, whereas before she wasn't eating much... She's allowed to drink as much as she wants. Her kidneys, she's got almost 50% of kidney function now, which is incredible. She's always going to need to take medication, but it's nothing compared to what she had… We've taken her abroad whereas before I would have never dared to go anywhere with her. Our lives were really very difficult... Now we are having a normal life, as normal as possible. Then, we lived each day at a time. Now, we can make plans.

Adult A

Adult A was 63 when diagnosed with aHUS. She was given plasma exchange treatment in hospital every day initially. She describes her experience of this treatment as follows:

I just found it horrendous to be honest, because I found this treatment very intrusive…At first I was very sick while I was on it, then another day I had a full anaphylactic shock, and some days my blood pressure would just suddenly drop, and I'd have to be quickly taken off the machine…I came out in rashes, I had hives which spread down my whole body or other days it would be big red lumps, I didn't know how I was going to react each day… we were like rabbits in the headlights, we didn't know whether we were coming or going… And at the same time I was filling up with fluid, I put on about 2 stone in weight, and it was fluid, so my legs were like tree trunks… I didn't have lot of energy, I couldn't wash properly, because the tubes were sticking out of my neck, there's always a risk of infection, so I couldn't go in the shower as normal, I couldn't wash my hair… my legs were so full of fluid I couldn't bend them to wash and dry my feet. Simple things like that were such a big chore…

After several weeks she returned home and continued to receive plasma exchange at the hospital every other day. She received 65 treatments over a course of six months. The side-effects were reduced but she did not feel completely well.

I was existing, once my plasma exchange was reduced, but I felt as though I was sitting on the sidelines watching all this going on. It was an odd feeling. I went through the motions, I gradually was able to do more, go out for little walks, go for lunch with friends, but it wasn't my life back again.

She was then entered onto the Eculizumab trial. She now receives an infusion for 35 mins every two weeks and has stopped the plasma exchange.

After a few weeks on Eculizumab the tubes were taken out and that was a big, big day for me, it was wonderful. The Eculizumab is so much easier than the plasma exchange was… I cannot find the words to stress the huge, huge difference it has made to me and my family; it's just given me my life back. Instantly I felt a difference, but you gradually over the months do feel stronger, and you think, ooh, I can do such and such and I haven't been able to do that for a while, and walking further, doing more, it has just been wonderful, absolutely wonderful. We've now been away for a week; for weekends and we can do that sort of thing…I am doing loads more now. I've got my independence again.

6.2 Patient/ carers expectations of Eculizumab

Patients with renal failure

Patients with aHUS who have kidney failure are facing the prospect of remaining on dialysis for the rest of their lives. Eculizumab offers the potential for a kidney transplant, and therefore restoration of their health and a life free from the restrictions of the treatment.

> *All of a sudden there's a possibility of a drug which could mean I could have a transplant and what I see as having a normal life again. My husband could work, I could possibly work. We could go away and see my husband's family who live miles away. I'd love to be able to jump in a car and be spontaneous… I'm not saying a transplant is the be all and end all. It isn't easy. But dialysis is hard for me and for everyone else.* (**Patient)**

> *It is difficult to plan for the future, because the future is dialysis ;but all of a sudden ,now there's a little bit of light at the end of the tunnel, and I think that's the future that is what we have got look for now.* **(Partner)**

For partners/ family members/ carers, the possibility of a transplant would also be life-changing, giving them more time, less responsibilities and reducing their anxiety. Some find it hard to imagine and to some extent are fearful of the consequences. They have adapted their lives around the condition for many years and have been through hopeful times only for the disease to come back again. They believe it would take them some time to feel confident that the drug was really working.

> *If the drug came in, the change would be immeasurable really it would be massive. We'd have to get our confidence up – I can't imagine it now. The stress would be better – we'd all sleep better – but I don't think we could shake it all off – there would always be a bit of you thinking I wonder if it's going to go wrong…* **(Partner/ Family member)**

Opening up the possibility for kidney transplants also means parents and family members will be faced with difficult decisions about whether to donate a kidney to the person with aHUS. Donating a kidney is not without its risks. It involves a major operation and women of child-bearing age are advised not to donate their kidney if they want to have children. However, because there is a waiting list for transplants, there is always a fear that the person with aHUS may become sicker or even die while waiting for a suitable donor. This can place enormous pressure on individuals and family relationships.

Patients with active disease

The disease is currently suppressed in these patients with continued plasma exchange, although this does not always prevent relapses. This treatment is time consuming, can make people ill and is associated with risks of line infection. If people continue to relapse they are still at risk of losing their kidney function over time.

Eculizumab offers the possibility of avoiding end stage kidney failure, dialysis and kidney transplants as well as any other organ damage. It offers patients the chance of retaining whatever residual function they have in their kidneys without the need for further treatment and may sometimes restore some kidney function.

Patients in remission or with known genetic risk of aHUS

For these patients and their partners or families, the concern is always that the disease could start or reoccur at any time leading to kidney or other organ damage. Families affected in this way live with a great deal of anxiety. Eculizumab takes away a lot of this fear.

> *If you imagine that your child could become ill anytime and that it could affect his kidneys, his brain, his lungs – anything and there's no cure for it – that's bloody scary to live with. To then find out there's now a drug that will stop it in its tracks – I can't tell you how that feels – it's elation really – it makes living with it bearable. It gives you hope when there wasn't any hope.* **(Parent)**

For couples where one partner is affected by the gene, knowing Eculizumab was available would influence their life choices.

> *There's the possibility when I have children they can do tests during the pregnancy to see of the child carries the aHUS fault – and if it did, that would be a decision we would have to make. If we knew the drug was available for that child – that would be a positive for us.* ***(*Partner*/* Family member)**

APPENDIX A SUMMARY:BURDEN OF CURRENT CONVENTIONAL TREATMENT

The following summary of the burdens of current conventional treatments was included in aHUSUK's patient submission to the Clinical Priorities Advisory Group and elicited from information supplied in the Life Experience Report and from an on-line survey completed in May 2013 by aHUSUK members. To fully appreciate the huge improvement in treatment that eculizumab brings it is necessary to understand the two existing treatments.

1. PLASMA EXCHANGE

"In recent years plasma exchange (PEX), that is the replacement of the body's entire blood plasma in one session, has been the standard pre-dialysis treatment for adults and children. It is not pleasant. Patients have told us about daily treatment sessions lasting several hours.

The side effects and risks as follows:

• Oedema causing shortness of breath and mobility problems ,
• Hives, allergic reactions and anaphylactic shock,
• Hypotension,
• Nausea and fatigue ,
• Inconvenience and risk of fixed lines becoming dislodged or causing infection.

Although there were occasional reports of patients going spontaneously into temporary remission, these are rare, and when PEX failed to maintain kidney function, as it often did over the longer term, dialysis was the only remaining option.

2. DIALYSIS

Dialysis is required when kidney function is lost. It is a replacement therapy and not a complete substitute for a functioning kidney. Patients are subjected to a strict diet and fluid restrictions of 500 ml a day. Dialysis can be done in hospital or at home. Many patients resigned to a lifetime of dialysis prefer the flexibility of being able to dialyse at home; but that requires space, equipment and training in its use. All patients found treatment a huge burden.

They reported the physical and mental effects as follows:

• Requirement for operations to create access points for treatment and surgery to maintain effective fistulas and avoid catastrophic bursts, but knowing that these access points are finite;
• Risk of tesio line in jugular vein becoming infected, splitting or becoming detached;
• Those dialysing with a fistula having to place two large and sharp needles into their own arm;
• CAPD dialysis requires a permanent catheter into the abdomen, which results in scarring and body image issues
• Having to cope with technical faults/power cut/water supply issues in the equipment in mid treatment on home dialysis (with the risk of losing 400ml of blood volume)
• Constant vigilance required to spot infection and possible air entry into lines
• On CAPD it is inconvenient and tying to exchange dialysis fluid every four hours every day
• Extremely low blood pressure causing patients to 'crash 'and lose consciousness during treatment
• High blood pressure causing seizures and migraine headaches
• Cramps, nausea, faintness and/or headaches during and following a dialysis session

• Fatigue due to anaemia and requiring blood transfusions or self injection of EPO
• Fear of fluid overload causing respiratory failure and drowning in your own body
• Fear of potassium levels so high they can cause a heart attack
• Greater risk of heart and blood vessel disease including strokes and fluid around the heart and severe damage to the heart valves requiring open heart by-pass surgery
• Steal syndrome associated with fistulas causing pain and requiring surgery
• Losing hair because of blood thinning drugs required for dialysis
• Episodes of extremely painful and life threatening peritonitis
• CAPD treatment causing encapsulating Sclerosing peritonitis which requires major abdominal surgery and on-going treatment which can cause ovarian cysts
• Anxiety and depression resulting in need for counselling and medication
• Body image problems resulting from scarring and from unsightly fistulas and from weight gain and loss from treatment
• Parathyroid problems
• Pulmonary Hypertension
• Carpal tunnel syndrome
• Gall stones and gall bladder removal
• Renal bone disease causing joint pain and need for hip replacements
• Restless legs syndrome
• Dry and extremely itchy skin
• Impaired cognitive function
• Coping with aftermath of miscarriage and premature births during episode of aHUS.”

APPENDIX B

Methods used to develop the Patient Experience Report*

M1 What methods were selected and why

One-to-one interviews were used to gather the information for this patient submission. This method was chosen because aHUS UK members had stated they would prefer this approach to focus groups. This method also ensured that:

- in-depth, qualitative findings about people's experiences of aHUS were obtained
- interviewees felt comfortable talking about sensitive and distressing topics
- the work of aHUS Action was not duplicated through repeating a survey

Although preparation of this submission did not require formal ethical approval, the principles of good ethical practice were still applied, for example, by addressing issues of confidentiality and ensuring interviewees were fully informed about the project before agreeing to take part. Helpline support was made freely available to the interviewees so that they were able to obtain professional support if they became distressed as a result of taking part.

M2 How participants were selected and recruited

A purposive sample of interviewees was selected to ensure that the full range of experiences of aHUS was captured through the interviews, as well as the most common experiences of the condition. Parents, partners and other family members were also interviewed to understand how the condition affects their lives.

A brief review of the literature was conducted via an internet search, drawing mainly on reports of patient experiences from international patient organisation websites[2]. Advice was also sought from aHUS UK Trustees and Professor Tim Goodship on the most common experiences of aHUS. The sample was then chosen to include:

1. Patients with different ages of onset. aHUS can affect people at any age, but there appear to be peaks in the numbers of people affected at a young age (0-6), in their early twenties, and after the menopause in women. Patients were therefore selected within these peak age ranges.

2. Patients and other interviewees of both genders. More women were interviewed than men, which may partly reflect the greater incidence of aHUS in females, or different individuals' willingness to contribute to this submission.

3. People with experience of the different outcomes of the disease. In terms of the impact on kidney function, this included patients with no kidney damage through to patients with end stage renal failure. Others were included with experience of aHUS damage to other organs, or loss of family members with aHUS.

[2] http://ahus.org.uk/
http://atypicalhus.50megs.com/
http://atypicalhus.ning.com/page/a-parents-perspective-ahus
www.rarediseasecommunities.org/en/community/atypical-hemolytic-uremic-syndrome-ahus

4. People with experience of the different types of treatment used to manage the condition, including plasma exchange, different kinds of dialysis and kidney transplant.

5. People who have experienced the impact of the hereditary nature of the condition and the effects on the wider family.

aHUS UK contacted their members and recruited a total of 16 people, who as a whole were able to contribute information about the most common experiences of aHUS across these different dimensions. Professor Tim Goodship was consulted and confirmed that this sample would be illustrative of the most common aHUS experiences.

At the time the interviews were carried out there were four patients (2 adults and 2 children) known to aHUS UK who had been given Eculizumab. One of the adults and parents the two children were available for interview and included in the sample. The characteristics of the interviewees are listed in Table 1, without any personal information so as to maintain anonymity.

Table 1: Characteristics of the interviewees

Age/ gender	Interviewee	Patient/family experience
Baby girl, aged 9 months	Mother	In remission after treatment with Eculizumab.
Child	Mother	4 children who died as a result of aHUS, 3 as babies, 1 at age 7.
Child – (boy aged 2)	Grandmother	In remission after plasma exchange. Grandmother lost 2 of her own children to aHUS as babies.
Child (girl aged 5)	Father	Receiving dialysis at home, awaiting transplant, receiving Eculizumab.
Child (girl aged 7)	Mother	Receiving plasma exchange and on long-term dialysis
Young person (boy aged 13)	Mother	In remission.
Young female adult	Patient and sibling (2 interviews)	Has end stage renal failure and is receiving dialysis at home. Transplant failed. Working.
Young female adult	Patient and husband (3 interviews)	Has end stage renal failure and is receiving dialysis at home. Transplant failed. Retired due to ill-health.
Young female adult	Patient and husband/daughter (3 interviews)	Has end stage renal failure and is receiving dialysis in hospital. Transplant failed. Retired due to ill-health.
Adult late onset – female	Patient	In remission after treatment with Eculizumab.
Adult late onset - female	Patient	Has end stage renal failure and is receiving dialysis at home. Transplant failed.

M3 Conducting the interviews and analysing the transcripts

A participant information sheet and semi-structured interview schedules were developed with input from aHUS Trustees and NSCT staff. The questions were designed with the aim of completing the different sections of the patient submission template. A pilot interview was conducted with an aHUS Trustee who also gave feedback on the process.

The interviews were arranged at a time and date to suit the interviewees and carried out in person (n= 12) or on the phone (n=4). With the interviewee's permission each interview was recorded. They were then transcribed in full and interviewees sent an anonymised copy of the transcript (all names and places removed) to check for accuracy and confirm they were willing for their quotes to be used in the submission.

All transcripts were read and analysed by both interviewers (See Section 7.4) who identified key themes. These related to the topic areas specified by the patient submission template. The transcripts were annotated to index the findings relevant to each of these agreed themes. This data was then collated and arranged into themes/ topics and used to generate a draft report. An early draft was discussed with the aHUS Trustee with the lead on this submission. A subsequent draft was discussed with all of the aHUS Trustees at one of their Board meetings. Their feedback was taken on board and the next draft reviewed by Professor Tim Goodship (solely to check for clinical accuracy) and by NSCT staff. A copy of the final report was sent to all the interviewees.

This work was completed between 21 March and 14 May 2012; and 19 January 2013.

M4 Declaration of any conflict of interest

This submission was prepared by aHUS UK with support from TwoCan Associates. TwoCan Associates is a small company specialising in promoting patient and carer involvement in health and social care. The two Co-Directors of TwoCan, Bec Hanley and Kristina Staley, conducted the interviews, carried out the initial analysis of the data and produced the first drafts of the report. Further information about TwoCan is available on their website www.twocanassociates.co.uk

There were no conflicts of interest amongst any of the individuals who contributed to this submission.

* **Additional patient evidence was collected from interviews conducted with a group of four aHUS patient and family members from Wales. The same methodology was used except the interviews were conducted in a group context.**