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A comparative study on living with atypical haemolytic uraemic syndrome: Was patient experience better in 2024 than in 2014?

Len Woodward

len@ahusallianceaction.org

aHUS Alliance Global Action

Linda Burke

aHUS Alliance Global Action

Kamal Shah

aHUS Alliance Global Action

Research Article

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A comparative study on living with atypical haemolytic uraemic syndrome: Was patient experience better in 2024 than in 2014?

Len Woodward[1] ✉, Linda Burke[1], Kamal Shah[1]

[1]aHUS Alliance Global Action, Cheshire, UK

✉len@ahusallianceaction.org

Corresponding author: Len Woodward

Abstract

Background: Understanding patients' experiences of atypical haemolytic uraemic syndrome (aHUS) is essential for better care and support. aHUS is an ultrarare, life-threatening disorder caused by uncontrolled activation of the alternative complement pathway, leading to endothelial damage, thrombotic microangiopathy (TMA), acute kidney injury, and kidney failure. It requires specialist expertise for accurate diagnosis and effective management.

Methods: In 2014, the aHUS Alliance partnered with EURORDIS/RareConnect to poll the global aHUS community across five domains: diagnosis and genetics; treatment; information and support; societal impact; and access to centres of excellence, research and registries. In 2024, the Alliance repeated the poll to assess progress over the decade. Both used online questionnaires in English and several other languages to promote inclusivity. There were 217 respondents in 2014 and 296 in 2024. Responses were collated in Excel and compared using bar graphs.

Results: Respondents in 2024 were older and predominantly female. Diagnosis timelines decreased by 20%. While approximately 80% of patients underwent genetic testing in both surveys, results were obtained substantially faster in 2024 (47% within one month versus 17% in 2014). Access to effective treatment increased from 61% to 74%, driven by longer-acting complement inhibitors, whose use rose from 0% to 39% of patients. Sources of

information and patient support were transformed. Awareness of societal impacts increased slightly, but just over half of respondents reported no additional burden. Coverage of expert centres (approximately 50%) and participation in research and registries (approximately 33%) showed little change.

Conclusion: Across surveys conducted ten years apart, meaningful progress in access to complement inhibitors was observed, with patients living longer and the condition predominantly affecting females. Significant challenges remain, particularly the need for more rapid diagnosis to optimise outcomes. Emerging communication technologies could further empower patients in daily life. Only half of respondents reported societal impacts, highlighting the need to better understand long-term effects on education and employment. Greater research participation and regular experience tracking are essential to improve quality of life for people living with aHUS.

Keywords: aHUS, Complement System, Rare Disease, Global Survey, Patient Experience

Background

Patient experience is an important dimension in improving healthcare quality [1, 2]. Understanding the atypical haemolytic uraemic syndrome (aHUS) patient experience, from disease onset through to living with the condition long term, can therefore contribute to meaningful improvements in patient care [3]. The initial experience of an aHUS patient is typically that of a life-threatening illness requiring urgent diagnosis and immediate initiation of effective treatment to prevent irreversible organ damage, end-stage kidney disease, or death [4].

Few patients are familiar with aHUS before being diagnosed because it is exceptionally rare [5–7], with an estimated prevalence ranging from 2.3 to 10 per million [8]. aHUS is the least prevalent of the conditions classified as thrombotic microangiopathies

(TMAs) and accounts for approximately 2% of all TMAs [9]. This rarity adds diagnostic and management challenges that are not faced by patients with more common TMAs [10].

TMAs are pathological conditions characterised by endothelial injury leading to thrombosis (the formation of small blood clots) in the microvasculature, primarily arterioles and capillaries [11]. This results in microangiopathic haemolytic anaemia (fragmented red blood cells), thrombocytopenia (a low platelet count), and organ damage, which can affect any organ but predominantly involves the kidneys and brain [12].

TMA is not a single disease but an overarching pattern seen in various conditions, including thrombotic thrombocytopenic purpura (TTP), malignant hypertension, transplant-associated TMA, pregnancy-associated TMA, drug-induced TMA, STEC-*E. coli* haemolytic uraemic syndrome, and aHUS [13]. The key distinguishing feature of aHUS is that endothelial damage is driven by uncontrolled activation of the patient's complement system, which is part of the innate immune response, rather than by another primary condition [14]. aHUS is therefore classified as a complement-mediated TMA [15], and it is usually caused by one or more predisposing genetic variants in the components of the complement system that impair its proper function. However, a large minority of patients may acquire autoimmune antibodies that prevent control components from working properly or exhibit idiopathic disease with no genetic or acquired predisposing factor found [16, 17].

However, the triggering events that often precede an episode of aHUS, such as infections, pregnancy, malignancy, autoimmune diseases, organ transplantation, or certain medications, can also be frequently seen in other TMAs [18]. This is further complicated by other TMAs, which can also precipitate complement overactivation secondary to their own TMA [19]. Consequently, the diagnosis of aHUS typically relies on the exclusion of other causes of TMA [20], which can introduce critical delays when rapid treatment initiation — ideally within seven days of presentation — is essential for optimal patient health outcomes

[21]. The experience of living with aHUS largely depends on the level of kidney function the patient has retained, which impacts their ability to study, work, and play, and maintaining kidney function depends on the rapidity of diagnosis and access to complement inhibitor treatment [22].

In 2014, little was known about patients' experiences of having and living with aHUS. The aHUS Registry had begun recruiting patients, but other than a presentation of early data about patient characteristics at the American Society of Nephrology (ASN) Kidney Week in 2013, no global data were available [23].

Furthermore, no published research exists on patients' lived experience beyond indirect references to quality of life in clinical treatment trial reports [24]. Patient stories appeared on early advocacy websites and in brochures [25] or in unpublished qualitative evidence produced for a health technology review of aHUS treatment by the National Institute for Health and Care Excellence (NICE) and its predecessor, the Advisory Group of National Specialised Services (AGNSS) [26]. No quantitative studies have examined the broader lived experience, including matters such as the diagnostic journey, treatments, societal impact on families, or information and support needs [23].

A discussion on the EURORDIS/RareConnect aHUS community platform led to a collaboration between a new international aHUS patient advocacy organisation called the aHUS Alliance. Among the list of aspirations for the new organisation was "patient experience research" [27]. This took the form of a global patient poll with EURORDIS/RareConnect support [28], and the findings were intended to help advocacy groups raise awareness and improve access to treatment [29].

A questionnaire was developed by EURODIS/RareConnect with input from patient organisations from Canada, Spain, the UK, and the USA. It was structured around five key

domains known to be problematic for people living with rare diseases [30, 31], with the wider issue of societal impact added. The chosen domains were as follows:

- Achieving a correct diagnosis and accessing genetic testing
- Accessing and funding effective treatment
- Having the opportunity to benefit from a centre of aHUS excellence
- Participating in aHUS research and registries
- Understanding the societal impact on a family living with aHUS
- Meeting patient information and support needs

The first global aHUS patient characteristics and demographic data were also collected from the 2014 poll. The questionnaire was translated into five languages (Dutch, French, German, Italian and Spanish), used the Survey Monkey format and was hosted on the RareConnect platform from mid-February to early April 2014, yielding 217 responses from 17 countries. RareConnect produced an infographic [32], and an unpublished report was written for advocacy use [33]. A full set of pie charts of the results remained available online for eleven years before being removed by RareConnect after its closure, and only screen shots held by the aHUS Alliance remained [34].

The poll represented the first systematic effort to measure and quantify the patient experience of living with aHUS. However, while it was important to capture aHUS patients' lived experience in 2014, it is also important to track changes over time to identify both progress and remaining challenges [1]. For this reason, the aHUS Alliance Global Action repeated the poll in 2024.

Patient communities for only three diseases, Behçet's Syndrome, TRAP Syndrome and aHUS, conducted polls in partnership with EURORDIS/Rareconnect in 2014 [28]. To our knowledge, the aHUS patient community is unique in that it has repeated this global patient experience poll.

Methods

aHUS Alliance Global Action, a registered incorporated charitable organisation [35], planned to repeat the 2014 global poll of aHUS patient experiences in 2024 to compare and contrast the patient experience of living with aHUS between those two years. RareConnect was formally retired on 5th December 2023 [28]. Enquiries of an ex-employee of RareConnect established that no documents or files related to the 2014 poll remained. Therefore, volunteers from the aHUS Alliance Global Action would lead the 2024 poll project but first had to recreate the 2014 poll questionnaire to use in 2024.

To ensure comparability, the same structure of basic participant characteristics and rare disease lived experience themes of diagnosis and genetics, treatment, information and support, societal impact, and access to centres of excellence, research and registries was maintained. The aHUS Alliance Global Action had archived screenshots of the RareConnect pie chart presentation of the 2014 results and could therefore use them to recreate each question based on the titles and variables used in each of the twenty-eight pie chart figures [34]. Additional variable options were added to the multiple choice questions using the answers to the “any other” option in the 2014 poll.

Thirteen new questions were also added, but since there were no 2014 comparators, their results are not included in this report and will be used for internal patient advocacy purposes only. This draft of the proposed questionnaire was then piloted by four people (3 patients and 1 caregiver), and their feedback was used to improve clarity and utility. The final questionnaire is presented in Appendix A (Question stems only).

The English version was translated into eleven additional languages (Arabic, Chinese, Dutch, French, German, Hindi, Italian, Polish, Portuguese, Spanish, and Turkish) to encourage diversity in participation. The French, German, Italian and Spanish translations were conducted by Atlas Translation Limited, a professional translation service company with

a peer review protocol and certification [36]. The remainder were translated by native-speaking aHUS patient advocate experts from the UAE, Hong Kong/China, the Netherlands, India, Poland, Brazil and Turkey. All translations performed by professional translators were reviewed by patient advocates, and their recommended changes were incorporated into the final questionnaires. Two platforms were used to access the questionnaires. The aHUS Alliance Global Action website uses Google Forms to link to all language versions [37]. Wenjuan Xing (WJX.cn) format was used for Chinese participants, and the questionnaire was distributed via WeChat/Weixin.com [38].

Although no record of the opening and closing dates of the 2014 poll exists, a contemporary report described it as running from mid-February to early April, approximately 6 weeks [33]. The 2024 poll questionnaire was open online from 8th July to 18th August 2024 (42 days). Seasonal differences in a global poll were unlikely to affect overall response numbers [39].

After launch, awareness of the poll was promoted by the aHUS Alliance Global Action and other aHUS alliance international patient advocacy organisations on the social media platforms Facebook, X/Twitter, LinkedIn and Instagram. Direct mail was sent to people who had previously engaged with the aHUS Alliance Global Action and The Atypical HUS Foundation. Attempts to promote it in Europe via kidney clinical networks such as ERKNet [40] and Rare Renal [41] were unsuccessful.

As this was planned to be an anonymous, noninterventional, voluntary, online poll, i.e., a survey of the quality of patient experience of living with aHUS, no ethics approval and no waiver were needed. However, informed consent was required for participation. An information sheet was included at the beginning of the questionnaire to assure that participants' personal data would be secure, anonymous and confidential and to explain how the survey results would be used—primarily for internal advocacy but potentially for wider

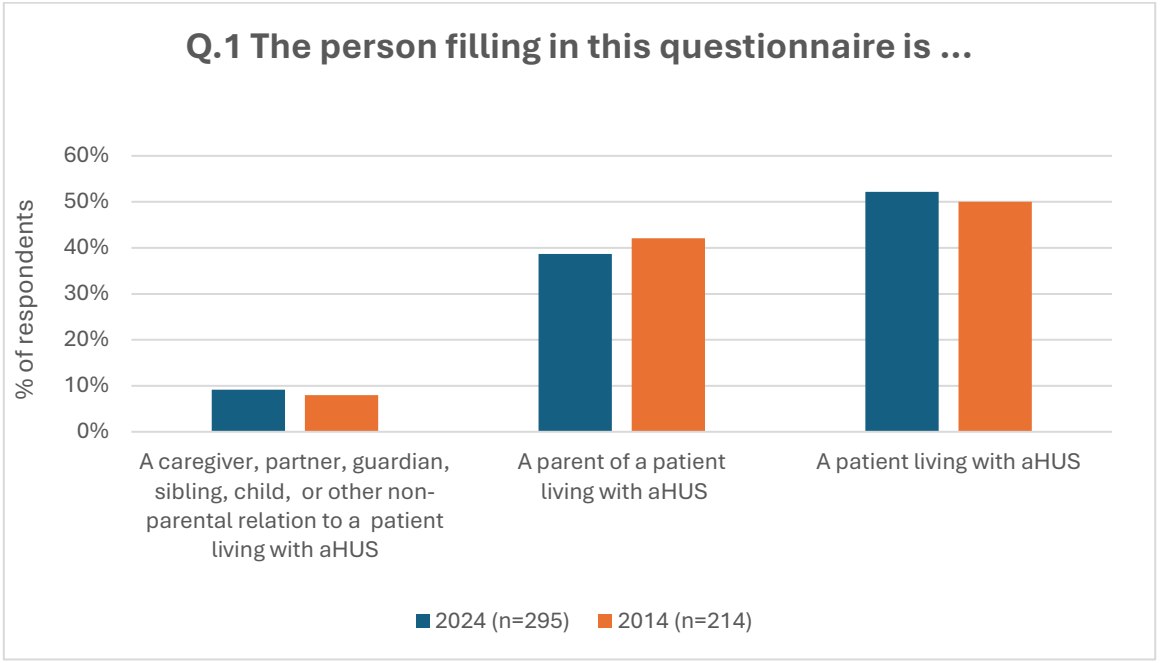
publication. Participants were given the opportunity to opt out of answering questions if they wished. The poll survey was open to patients diagnosed with aHUS and/or their parents and wider family members. The participants had to be 18 years of age or older. All respondents who did not expressly give consent were not included in the analysis or results.

The responses were downloaded to an Excel spreadsheet in English. This was done by first obtaining the response sheets in each language separately, then mapping each response to the corresponding response in the English survey (as each survey had exactly the same answer options for each question in exactly the same order) and then combining all the survey responses in one single sheet, which was used for analysis. An online translation service was used to translate the descriptive comments. The data were summarised, and the percentages for all answers were calculated. The 2014 pie charts from the Rare Connect screen shots in 2014, which had been manually adjusted for the previous “any other” category data, were used to provide revised numbers and relative percentages for 2014 and set alongside the 2024 data and comparative graphs produced.

Results

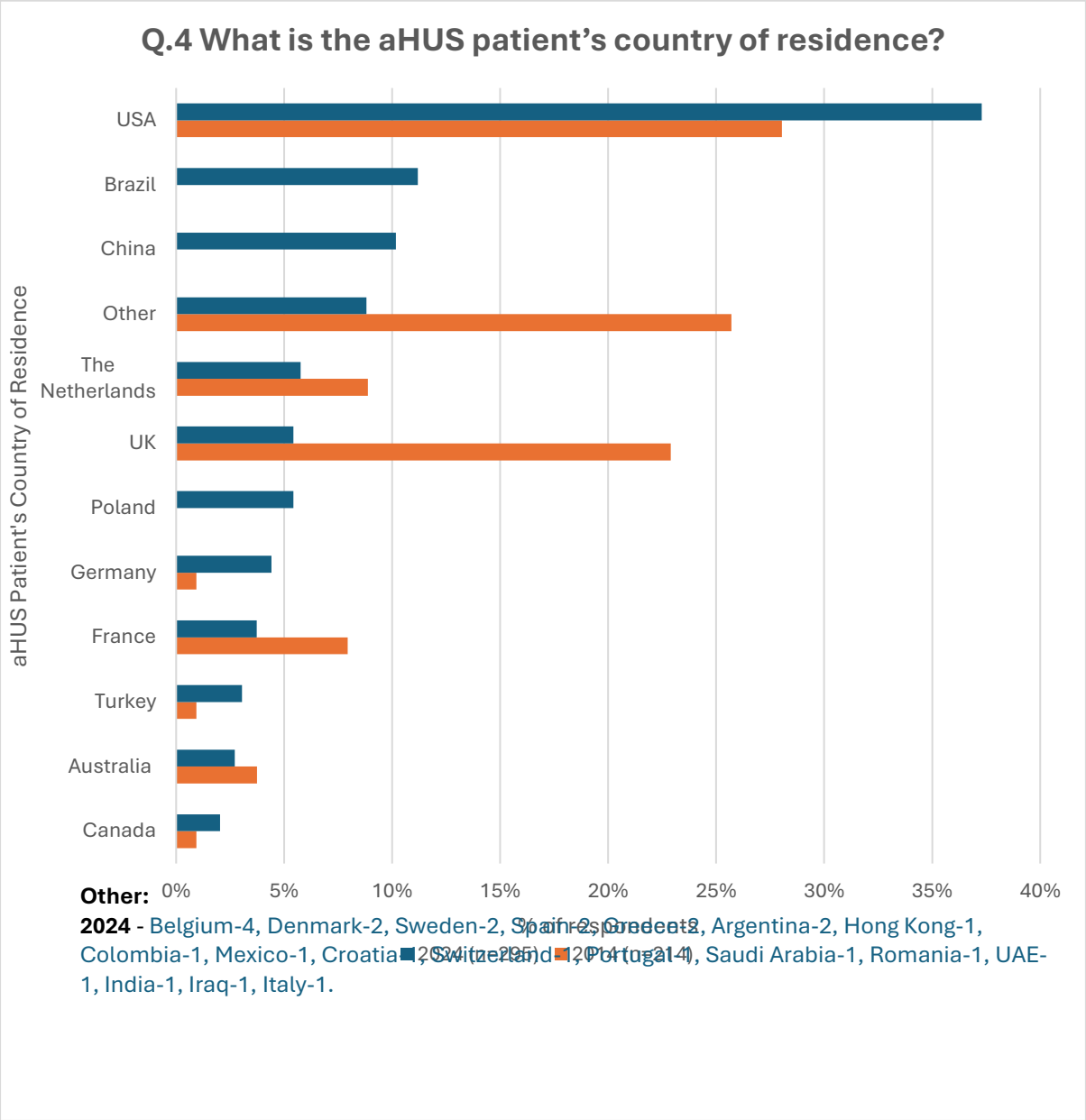
There were 320 completed questionnaires. However, 24 respondents did not complete the informed consent question and were therefore excluded from the analysis. This resulted in a final sample of 296 respondents for the 2024 survey. Although rare diseases typically affect multiple family members, participants in the 2024 survey were as follows: patients, 52%; parents, 39%; and other relatives and caregivers, 9% (Fig. 1a). This participation profile was very similar to that of the 2014 survey (50% patients, 42% parents, and 8% other relatives/caregivers). While relatives and caregivers remain underrepresented, the comparable mix between the two surveys supports meaningful year-on-year comparisons.

Figure 1a. The person filling up this questionnaire is



There were participants from 27 countries in 2024. The most common patient participant location was again the USA, making up approximately 37.5% of the 2024 total (Fig. 1b). Brazil and China had the second and third highest participation rates, respectively, and neither of these countries had participants in 2014. Noticeable decreases in the number of respondents were seen in European countries, particularly France, Italy, Spain, and the UK. Only Poland increased its participation from zero in 2014.

Figure 1b. Country of residence of aHUS patient



Twenty-eight Excel tables were created based on the survey responses. Of these, 27 comparative two-column charts are presented in this report. The remaining charts were reserved for internal patient advocacy use, as they either lacked 2014 comparative data or were not directly relevant to the patient experience. The results are presented in the following subsections:

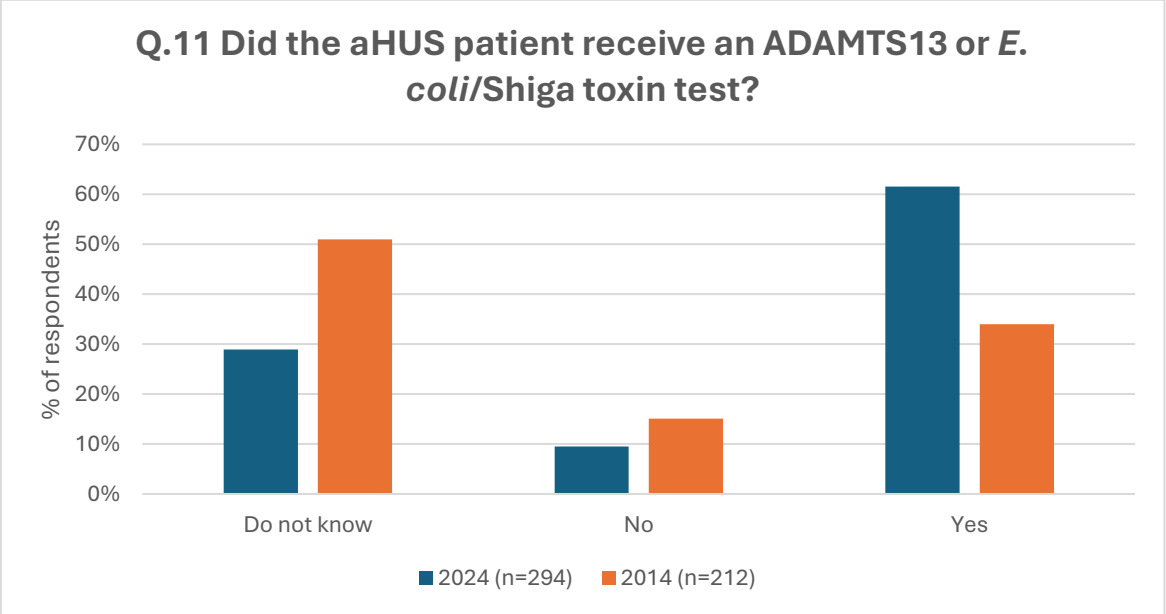
- Diagnosis Experience – Figures 2 to 11
- Treatment Experience – Figures 12 to 15

- Information and Support Experience – Figures 16 to 18
- Societal Experience – Figure 19
- Research Engagement Experience - Figures 20 to 23
- Gender and Age Experience – Figures 24a and b

Diagnosis Experience

Unless an aHUS patient has a known family history of the disease, the diagnosis usually marks their first encounter with this rare and life-threatening condition. aHUS is unfamiliar to most physicians. When TMA is suspected, the diagnosis proceeds by the exclusion of other TMAs, as no single clinical blood test or biopsy can definitively confirm aHUS. This section presents the patient's and caregiver's experience with the diagnostic process.

Figure 2. Did the patient have an ADAMTS13 or *E. coli* test?

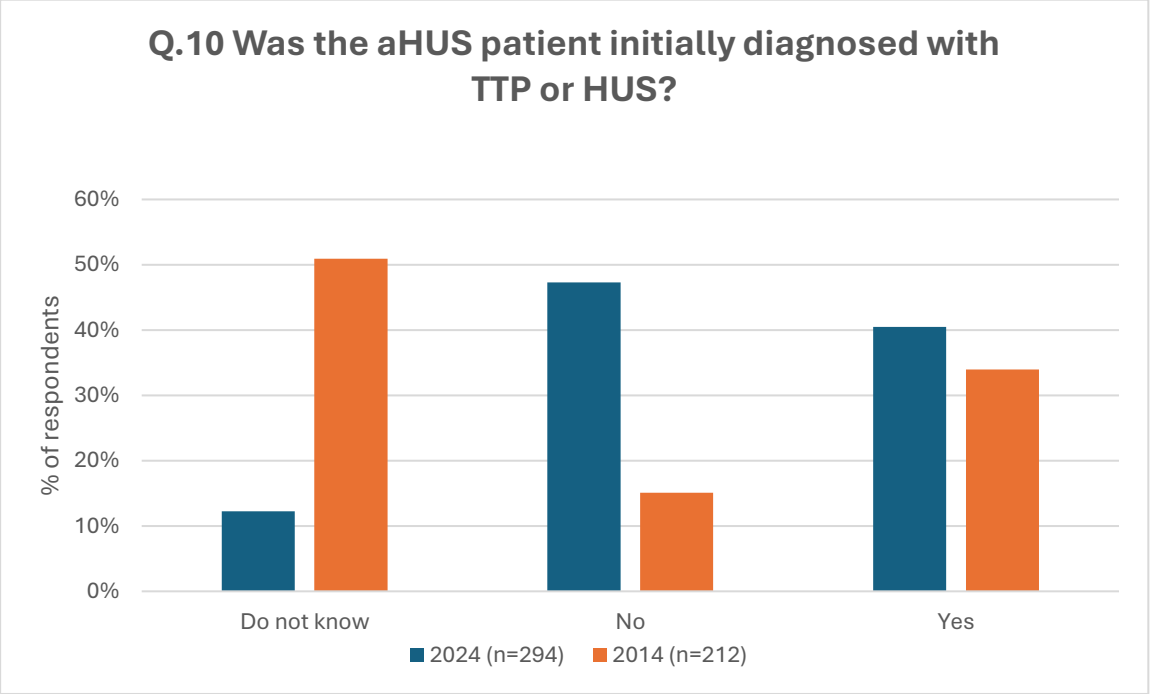


This question was asked because specific blood tests exist for other TMAs, such as TTP and STEC-HUS. Positive results for these conditions can help exclude them and support a more rapid aHUS diagnosis.

In 2024, 66% of the respondents reported that tests for other TMAs were performed (Fig. 2), a substantial increase from 34% in 2014. The proportion of patients reporting that no tests were carried out decreased from 15% in 2014 to 10% in 2024. There was also a large reduction in those who did not know whether such tests had been performed—falling from 51% to 29%.

Overall, patient experience with diagnostic testing for other TMAs has improved markedly over the ten-year period, with significantly more patients receiving appropriate tests and greater clarity about the diagnostic process.

Figure 3. Was the patient first diagnosed with TTP or HUS?

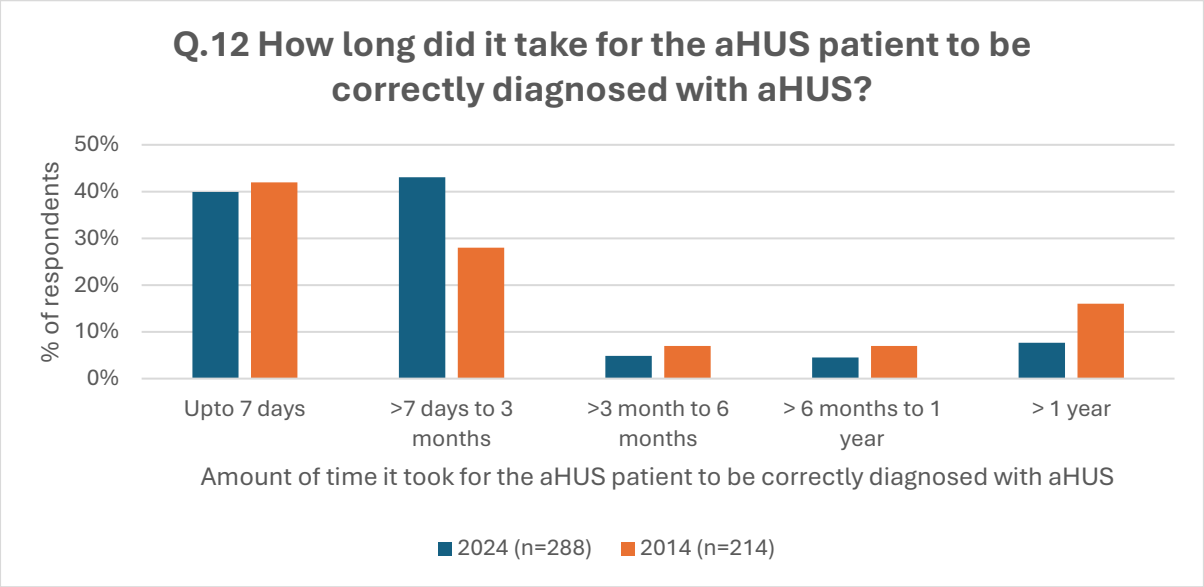


Misdiagnosis of aHUS can lead to delayed appropriate treatment, as conditions such as thrombotic thrombocytopenic purpura (TTP) and STEC-HUS present similarly but require different management strategies. Patients reported greater certainty about their diagnosis in 2024. The percentage of participants who were unaware of a potential misdiagnosis decreased sharply from 50% in 2014 to 12% in 2024 (Fig. 3). Among those who were aware of their diagnostic history:

- In 2024, 47% of the patients confirmed that they had no misdiagnosis, compared with only 15% in 2014.
- However, 41% of the patients reported experiencing an initial misdiagnosis in 2024, an increase from 34% in 2014.

Overall, although more patients now know whether misdiagnosis occurred, the proportion of patients who experienced an initial misdiagnosis has increased. Even when the diagnosis is eventually corrected, any delay, whether short or prolonged, can negatively affect clinical outcomes and patient experience.

Figure 4. Time taken to be correctly diagnosed with aHUS



The time between a patient's first presentation to a healthcare provider with signs of TMA and receiving a confirmed aHUS diagnosis can significantly influence clinical outcomes and overall lived experience.

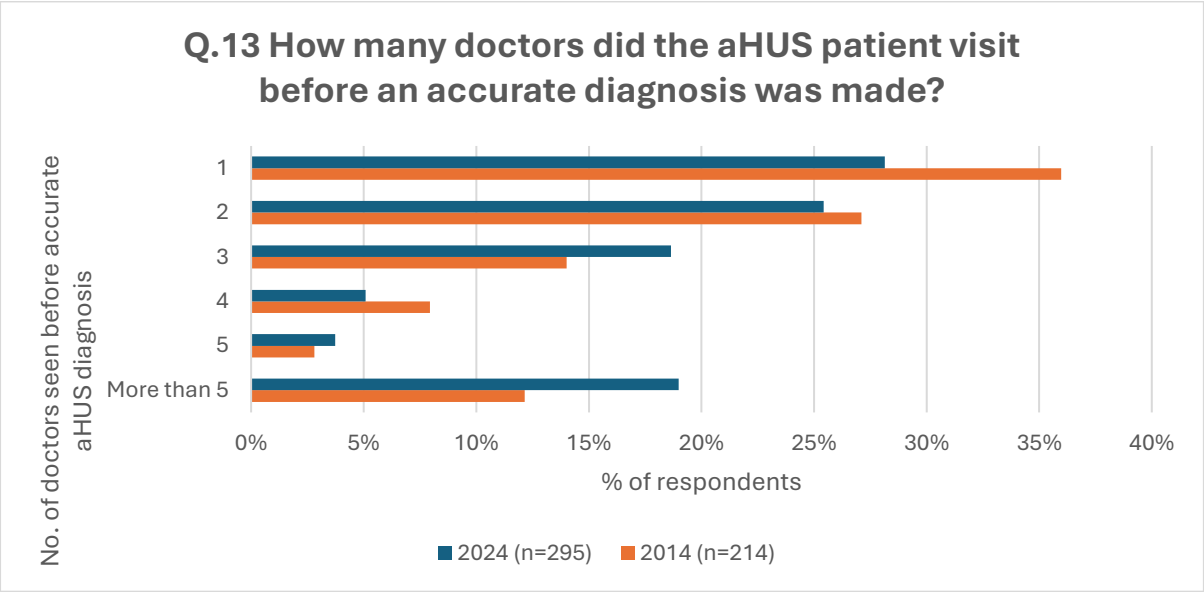
In 2024, 40% of the participants were diagnosed within 7 days of presentation, a slight decrease from 42% in 2014 (Fig. 4).

The proportion of patients diagnosed within up to 3 months increased substantially from 28% in 2014 to 43% in 2024. Moreover, the number of patients experiencing prolonged

diagnostic delays (over 3 months, including more than one year) decreased markedly, from a combined 30% in 2014 to 18% in 2024.

Overall, the diagnostic timeline improved over the ten-year period. While the proportion of very rapid diagnoses (≤7 days) declined slightly, there was a meaningful reduction in very long delays and a shift towards more patients being diagnosed within three months.

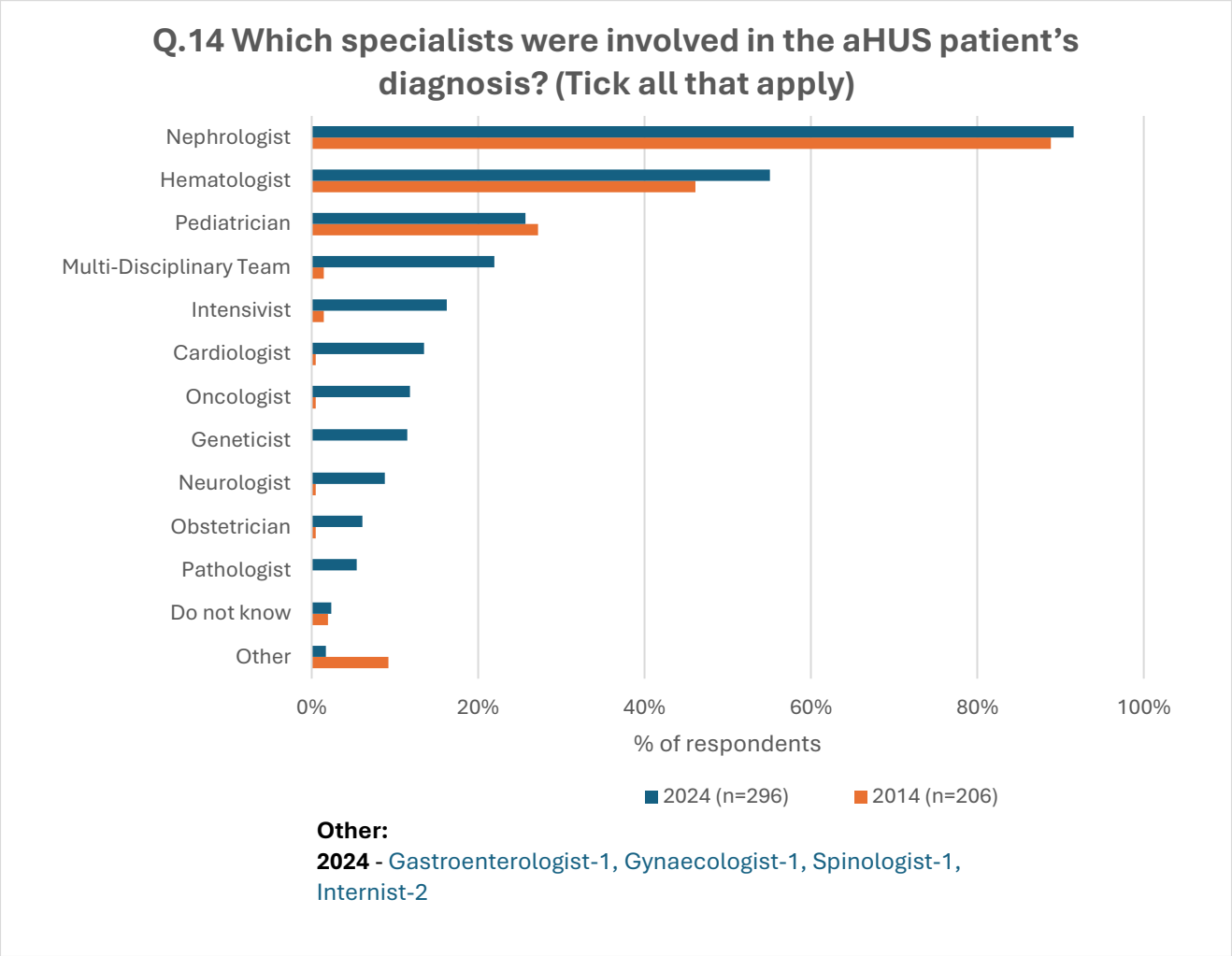
Figure 5. How many doctors were involved before aHUS was diagnosed?



This question was included because a common challenge in rare disease diagnosis is the number of doctors that patients must consult before receiving a correct diagnosis and starting the treatment. In 2024, 28% of participants reported receiving their aHUS diagnosis after seeing just one doctor—down from 36% in 2014—but this remained the most common experience (Fig. 5). A further 27% (compared with 25% in 2014) saw two doctors. Taken together, more than half of the respondents (55%) in 2024 were diagnosed with aHUS after consulting no more than two doctors. The percentage of patients who saw 3, 4, or 5 doctors before diagnosis increased slightly to 28% (up to 3 percentage points from 2014). However, the number of patients experiencing a more complex diagnostic journey increased more

noticeably: 19% reported seeing more than five doctors, up from 12% in 2014. Overall, while the majority of patients are still diagnosed relatively efficiently (within two doctors), there has been a clear shift over the ten-year period towards greater involvement of multiple specialists in reaching an aHUS diagnosis.

Figure 6. Specialists involved in the patient's aHUS diagnosis



aHUS is a haematological, renal and other organ condition that shares a disease course with that of other TMAs. As a result, patients' initial presentation can be to a wide range of specialists. This question was included to explore the patient experience of the different specialists involved in their diagnosis. The participants reported the involvement of 14 different specialties (Fig. 6). Nephrologists remained the most frequently involved, reported by 92% of the respondents in 2024 (89% in 2014). Haematologists were the next

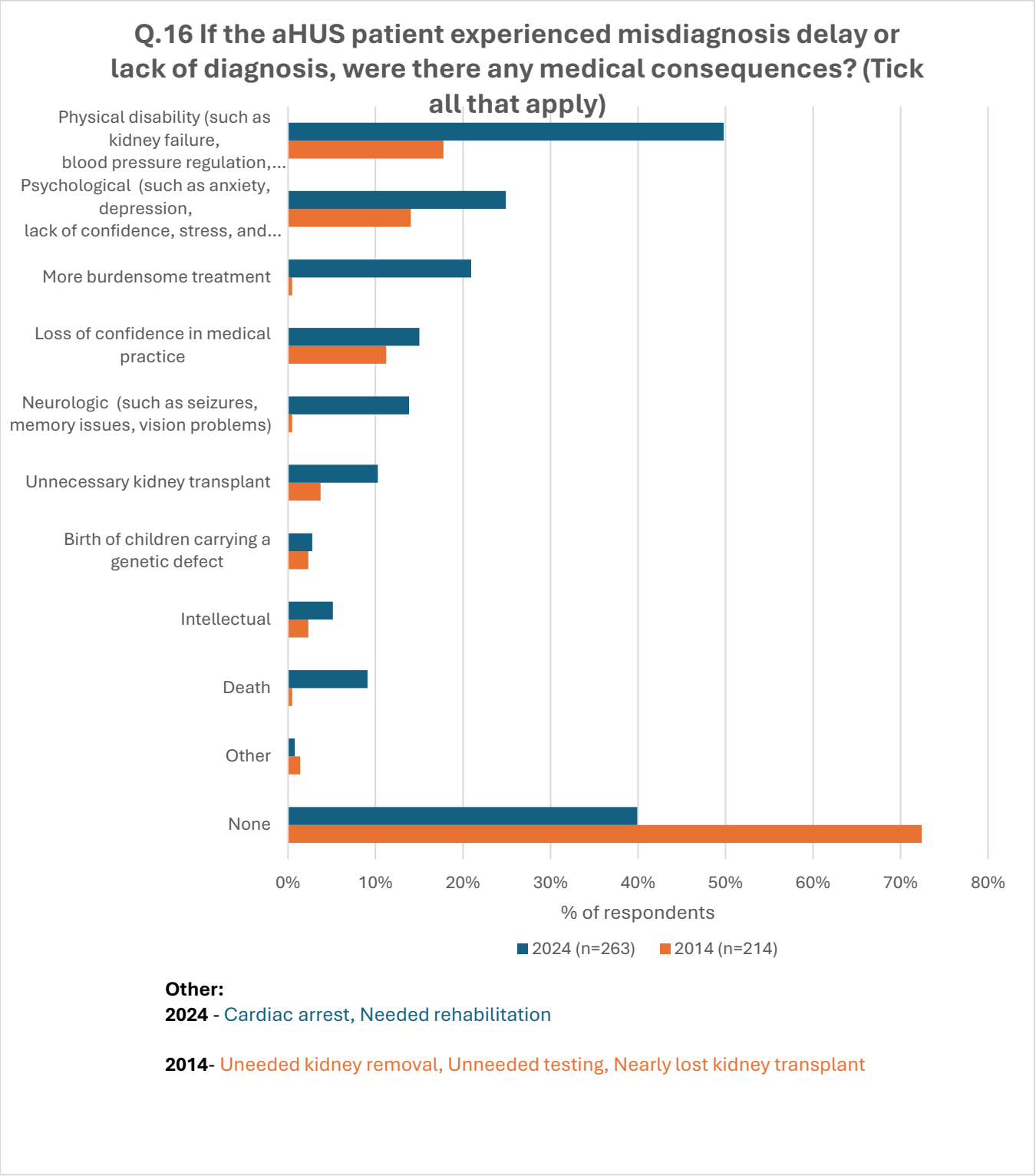
most common (55% in 2024 vs. 46% in 2014), followed by paediatricians (26% vs. 27%). There was little change in the proportion of participants reporting intensivists (16% in 2024 vs. 15% in 2014). Intensive care units are a frequent entry point into specialist care, and earlier identification of possible TMAs would benefit patients by enabling faster referrals to appropriate experts. Specialists involved in managing nonrenal organ involvement or disease triggers also increased notably between the two surveys:

- Cardiologists: 14% in 2024 (up from 0.5% in 2014)
- Neurologists: 9% in 2024 (up from 0.5%)
- Oncologists: 12% in 2024 (up from 0.5%)
- Gynaecologists (pregnancy-related aHUS): 6% in 2024 (up from 0.5%)

Supporting specialists also became more prominent. Involvement of pathologists (for blood tests and/or biopsies) increased to 6% (from 0% in 2014), and involvement of geneticists (for genetic testing and counselling) increased to 12% (from 0.5%). Other specialists included obstetricians.

No participants reported immunologist involvement in 2024. Multidisciplinary teams (MDTs) were reported by 22% of the respondents in 2024, a substantial increase from 1.5% in 2014. In summary, nephrologists, haematologists, and paediatricians remain the core specialists involved in aHUS diagnosis and management. Over the ten-year period, there was a clear increase in the involvement of other organ-specific specialists and, most notably, a much greater use of multidisciplinary team approaches.

Figure 7. Medical consequences of a missed or delayed diagnosis



This question was asked to understand the impact of delayed diagnosis or misdiagnosis on patients. Encouragingly, the proportion of respondents who reported no

adverse consequences (including no additional comorbidities or more burdensome treatment) increased significantly from 37% in 2014 to 57% in 2024 (Fig. 7).

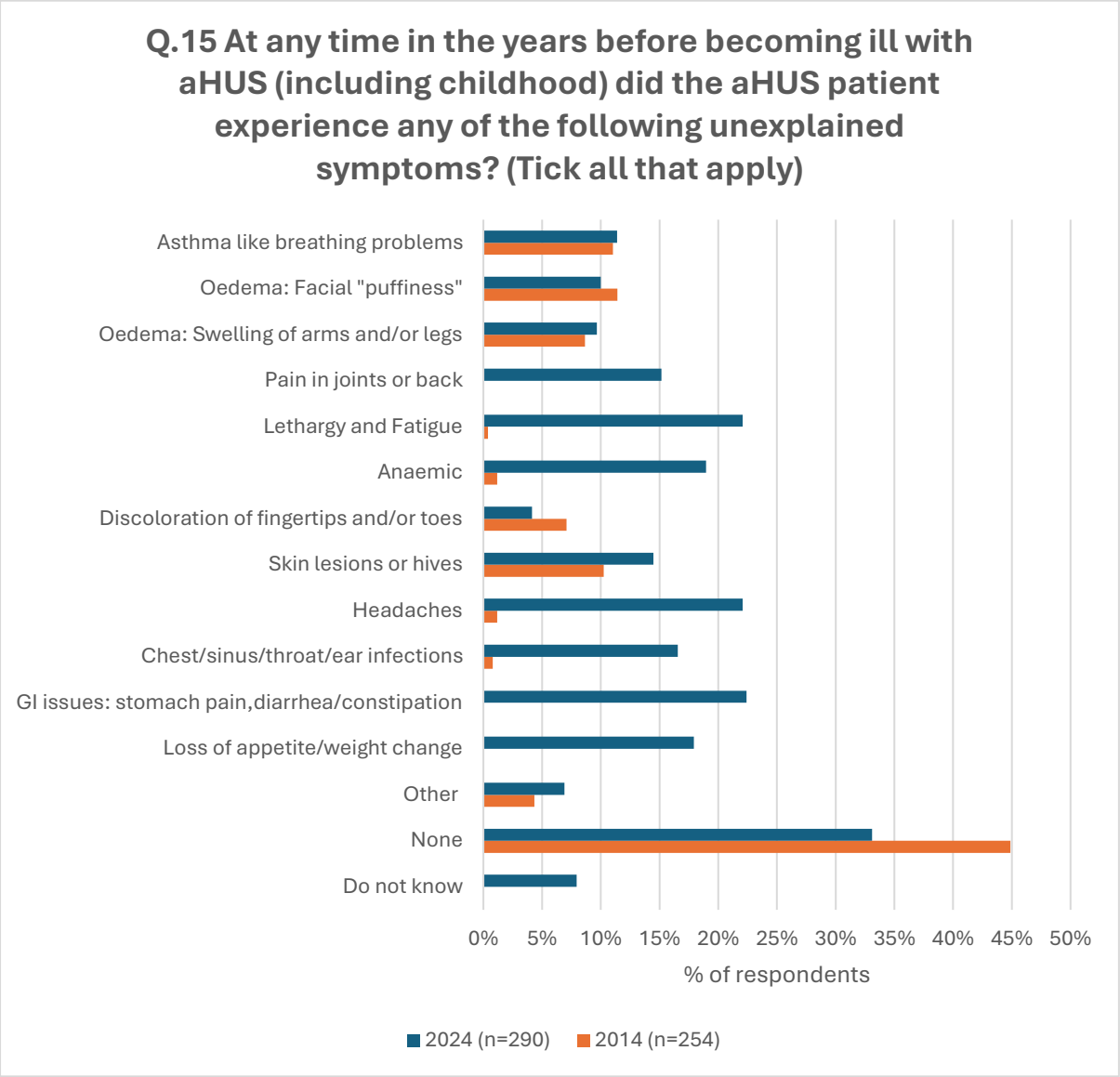
Among those who did experience consequences:

- The percentage of patients who died increased from 0% in 2014 to 8% in 2024.
- The frequency of physical comorbidities (such as kidney failure, hypertension, and eye problems) increased sharply from 14% to 48%.
- The prevalence of psychological consequences (anxiety, depression, stress, loss of confidence, and loneliness) increased from 11% to 24%.
- Neurological problems (such as seizures, memory issues, vision problems) were reported by 13% of the participants in 2024 (0% in 2014).
- The frequency of additional burdensome treatment increased from 0% to 20%.
- Unnecessary kidney transplants were reported by 10% of participants in 2024, compared with 3% in 2014.
- The prevalence of intellectual problems increased slightly from 2% to 4%.
- The percentage of patients who experienced a loss of confidence in the medical profession was also higher, increasing from 9% to 14%.

Overall, although a clear majority of patients in 2024 reported no lasting adverse effects, those who experienced consequences faced more severe physical, psychological, and treatment-related impacts than they did in 2014.

In particular, the reported rise in deaths predominantly reflected the experience of fifteen Chinese aHUS patients and is more representative of aHUS patients' outcomes before advancements in, and greater availability of, treatments that prevent such adverse events.

Figure 8. Unexplained symptoms experienced before becoming ill with aHUS



This question was asked to explore whether patients had experienced signs of subclinical TMA — episodes that did not progress to a life-threatening crisis but remained unexplained in their medical history. Awareness of such unexplained symptoms has increased since 2014. The percentage of respondents reporting no unexplained symptoms decreased from 45% in 2014 to 33% in 2024 (Fig. 8). The following symptoms were reported more frequently in 2024:

- Joint and back pain: 15% (0% in 2014)
- Lethargy and fatigue: 27% (0% in 2014)

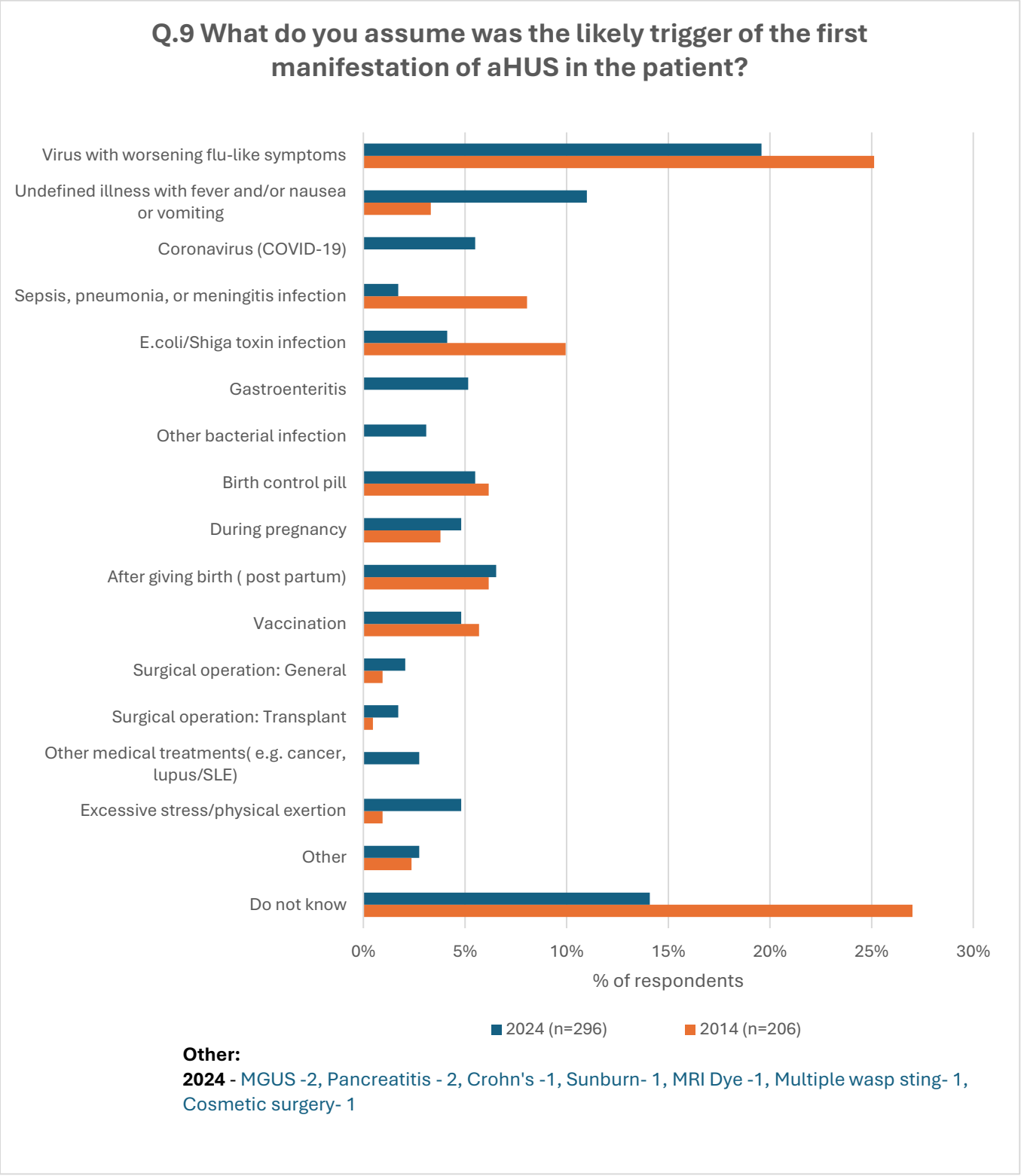
- Anaemia: 19% (1% in 2014)
- Headaches: 22% (1% in 2014)
- Chest, throat, sinus, or ear infections: 17% (1% in 2014)
- Gastrointestinal issues (stomach pain, diarrhoea, and constipation): 22% (0% in 2014)
- Loss of appetite or weight changes: 18% (0% in 2014)
- Skin lesions or hives: 14% (10% in 2014)
- Oedema in the arms and legs: 10% (9% in 2014)

Some symptoms showed little change or a slight reduction in frequency:

- Asthma-like breathing problems remained stable at 11%.
- Facial oedema decreased slightly (11% vs. 10%).
- Discolouration of the fingers or toes decreased from 7% to 4%.

Overall, the number of patient reports of unexplained common symptoms has increased since 2014. With the exception of anaemia and oedema, these symptoms were nonspecific and unlikely on their own to raise clinical suspicion of aHUS.

Figure 9. Triggering events for aHUS



An aHUS episode is triggered by an event that leads to uncontrolled complement activation. This question was asked to determine whether participants were aware of any known triggers preceding their aHUS onset. The percentage of respondents who did not know

what had triggered their aHUS decreased from 27% in 2014 to 14% in 2024 (Fig. 9), indicating greater awareness or a clearer recollection. Most frequently reported triggers in 2024 were as follows:

- Suspected virus with flu-like symptoms: 20% (down from 25% in 2014) — still the single most common trigger
- Undefined illness with fever, diarrhoea, nausea, or vomiting: 11% (up from 3%)
- Gastroenteritis: 5% (0% in 2014)
- Other bacterial infections: 5% (0% in 2014)
- Shiga toxin-producing *E. coli*: 4% (down from 10%)
- Sepsis, pneumonia, or meningitis: 4% (down from 10%)
- Coronavirus (COVID-19): 5% (new since 2014)

Collectively, infections remained the leading category, accounting for 54% of reported triggers in 2024 (up from 48% in 2014). The frequency of lifestyle-related triggers increased to 23% (from 17%):

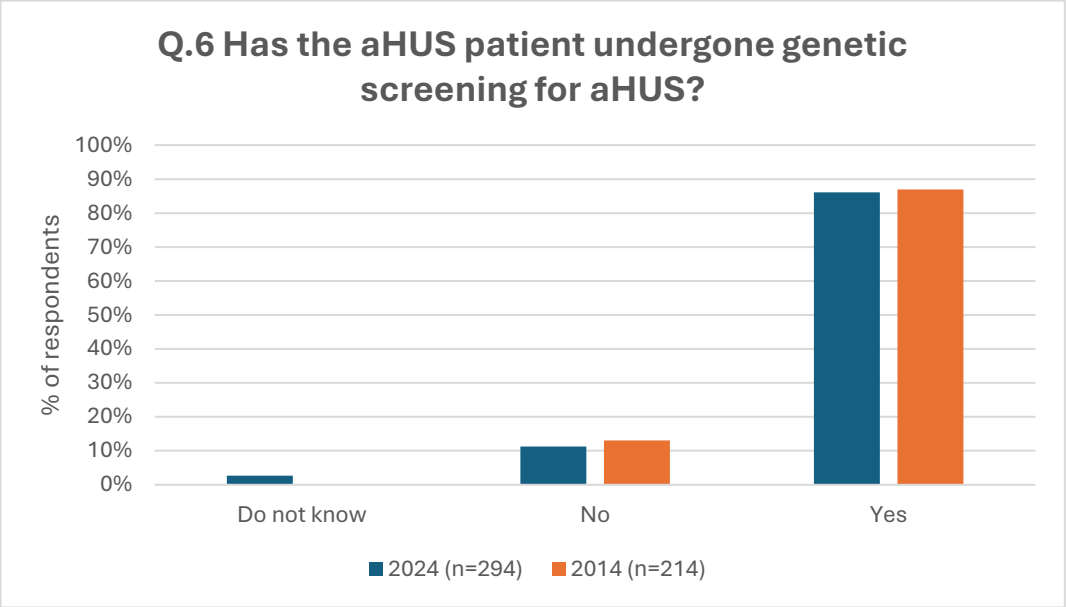
- Excessive stress or intense physical exercise: 5% (up from 1%)
- During pregnancy: 5% (up from 4%)
- Soon after giving birth: 7% (up from 6%)
- Oral contraceptive pill: 6% (unchanged)

The frequency of clinical event-related triggers increased to 12% (from 8%):

- Vaccinations: 5% (down from 6%)
- Kidney transplant and other surgeries: small increase of 1 percentage point each
- Secondary to treatment for other conditions (e.g., cancer or lupus/SLE): 3% (up from 0%)

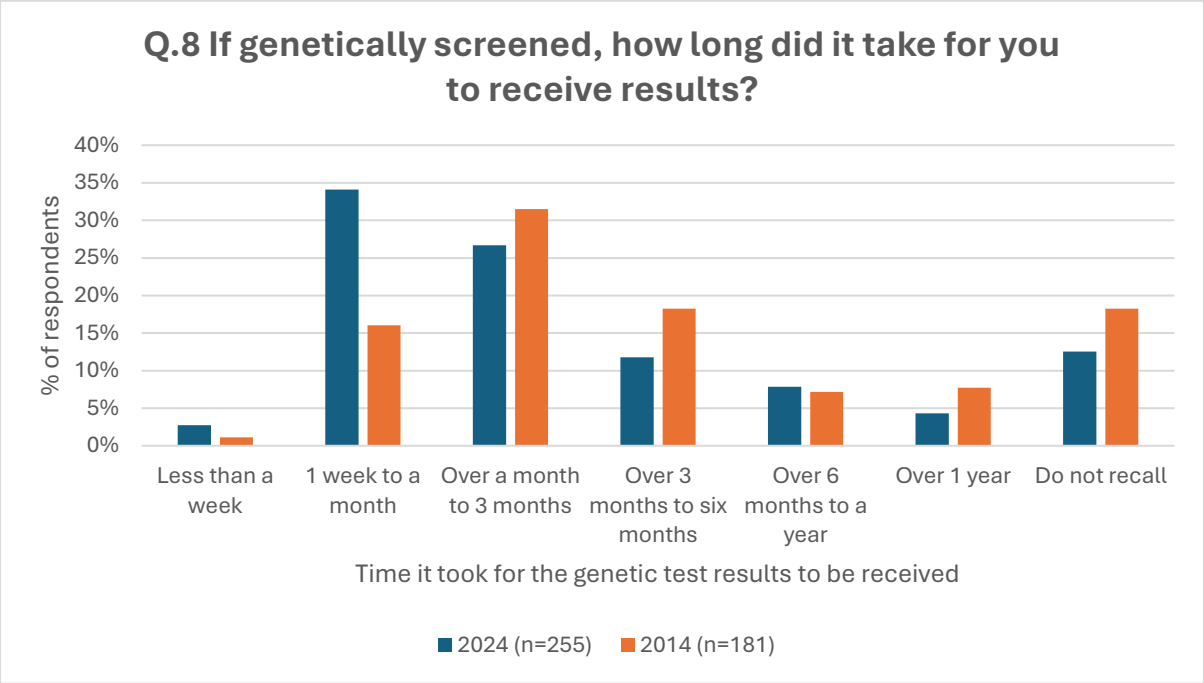
Overall, infections remain the dominant trigger for aHUS. There has been a modest shift towards more patients identifying lifestyle and clinical events as potential triggers, alongside a reduction in those who do not know what triggered their condition.

Figure 10. Has the patient had genetic testing?



Many rare diseases have a genetic cause, and genetic variants in the components of the complement system are known to cause the system to malfunction. Access to a laboratory that conducts genetic testing is not always available, and this question involves what aHUS patients have experienced in accessing tests. Most patients reported that they had been tested—86% in 2024 and 87% in 2014 (Fig. 10). Only 11% reported that they had not been tested in 2024, which is a decrease from 13% previously. A small percentage of participants reported that they did not know (3%). Therefore, there has been little change to testing access over 10 years.

Figure 11. Length of time to receive test results



Although treatment for suspected aHUS can begin before genetic test results are available, the time taken to receive those results remains important for confirming the diagnosis and guiding ongoing management. In the survey, participants were asked to recall how long it took to receive their genetic test results. In 2024, the percentage of participants who could not recall the timeframe decreased to 13%, from 18% in 2014 (Fig. 11). The most common reported timeframe was more than one week but less than one month, rising to 34% in 2024 from 16% in 2014. The share reporting one to three months declined slightly to 27% (from 32% in 2014). The percentage of patients who experienced longer delays also decreased:

- 3–6 months: 12% (down from 18%)
- 6 months–1 year: 4% (down from 8%)
- Over one year: 13% (down from 18%)

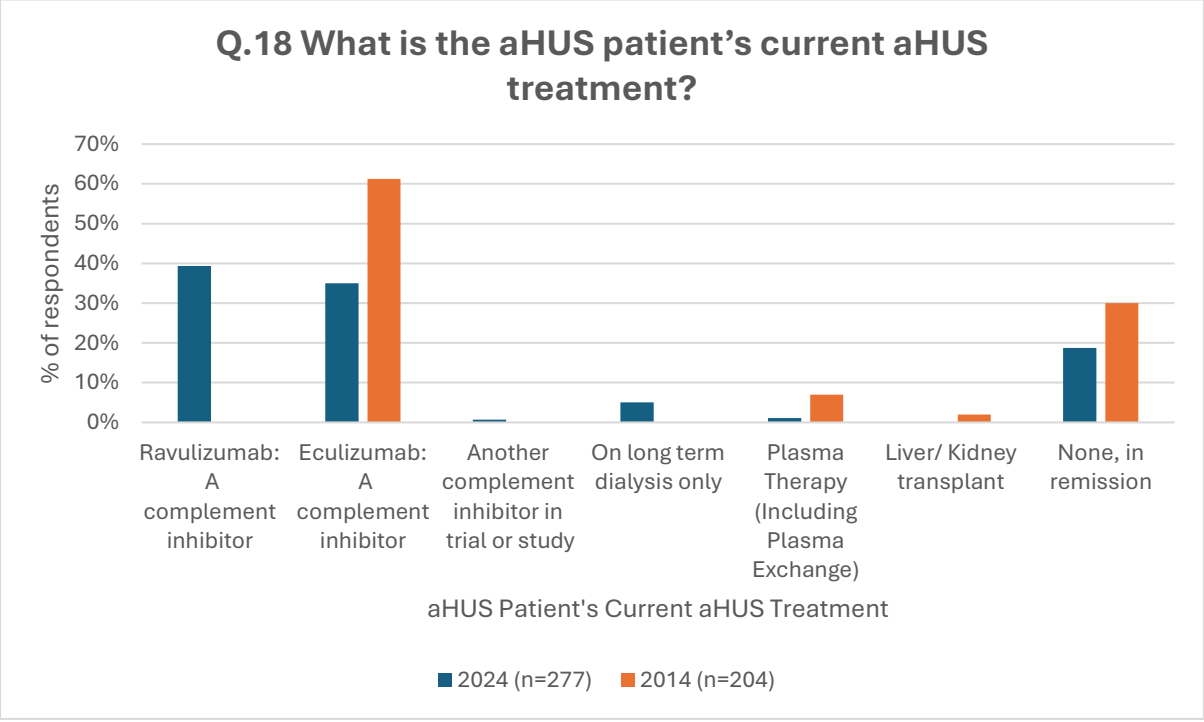
A small number of patients (3%) received results in less than one week in 2024, compared with 1% in 2015. Overall, there was a clear improvement in turnaround times. In 2024, 64% of patients received their results in less than three months, up from 49%

previously. These findings are clinically relevant, as genetic test results can influence decisions on whether to continue long-term treatment.

Treatment Experience

Treatment of aHUS focuses primarily on inhibiting the uncontrolled overactivation of the complement system. In cases of acute or chronic kidney failure, aHUS patients may require kidney replacement therapy (dialysis or transplantation). Kidney replacement therapy is generally more burdensome for patients than complement-inhibiting therapy is. The survey did not cover treatments for common comorbidities such as anaemia or hypertension. Like many rare diseases, effective treatments for aHUS are limited. Where effective therapies exist, they are often prohibitively expensive and may not be routinely commissioned or available in all countries.

Figure 12. What is the patient's current aHUS treatment?



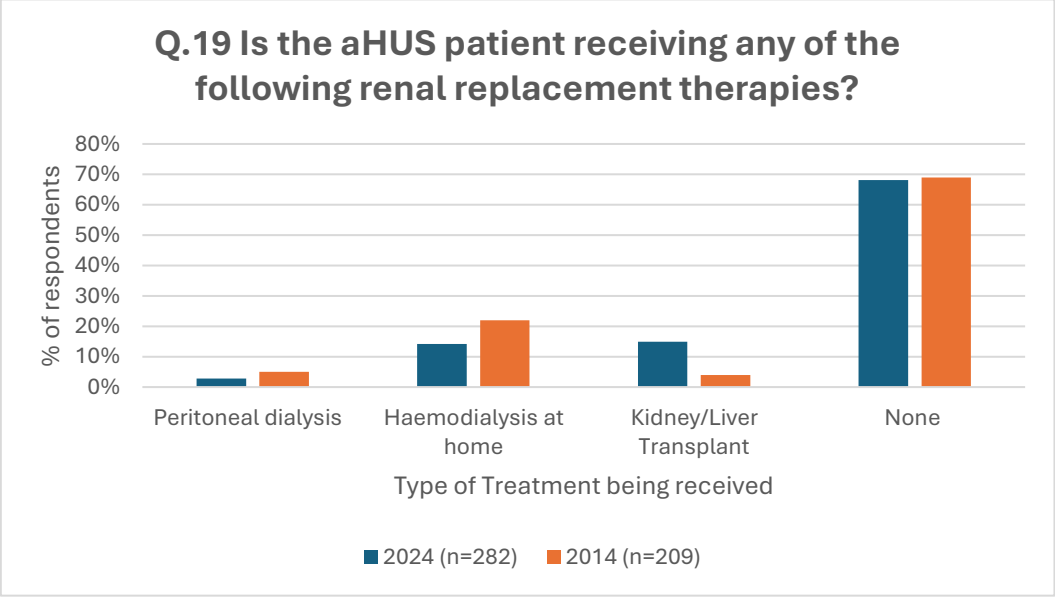
This question was asked to explore patients' current treatment experiences, with a focus on complement-inhibiting therapies.

In 2024, 74% of participants reported being treated with a complement inhibitor, up from 61% in 2014 (Fig. 12). Among these patients, most were receiving ravulizumab—a modified longer-acting version of eculizumab—whose frequency of use increased dramatically to 39% in 2024 (from 0% in 2014). Use of the original eculizumab decreased from 61% to 35% over the same period. Only 1% of participants reported being treated with another complement inhibitor as part of a clinical trial.

The use of other less common treatments decreased markedly: the use of other complement therapies, plasma exchange, and liver transplantation decreased from 7% to 2% and from 2% to 0%, respectively. The percentage of patients receiving only dialysis increased to 5% in 2024 (from 0% previously), while the percentage of untreated patients in remission decreased from 30% in 2014 to 19% in 2024.

Overall, complement inhibitor use has risen substantially over the past decade, with a noticeable switch from eculizumab to ravulizumab, while reliance on traditional, less effective therapies has declined.

Figure 13. Is the patient on renal replacement therapy?



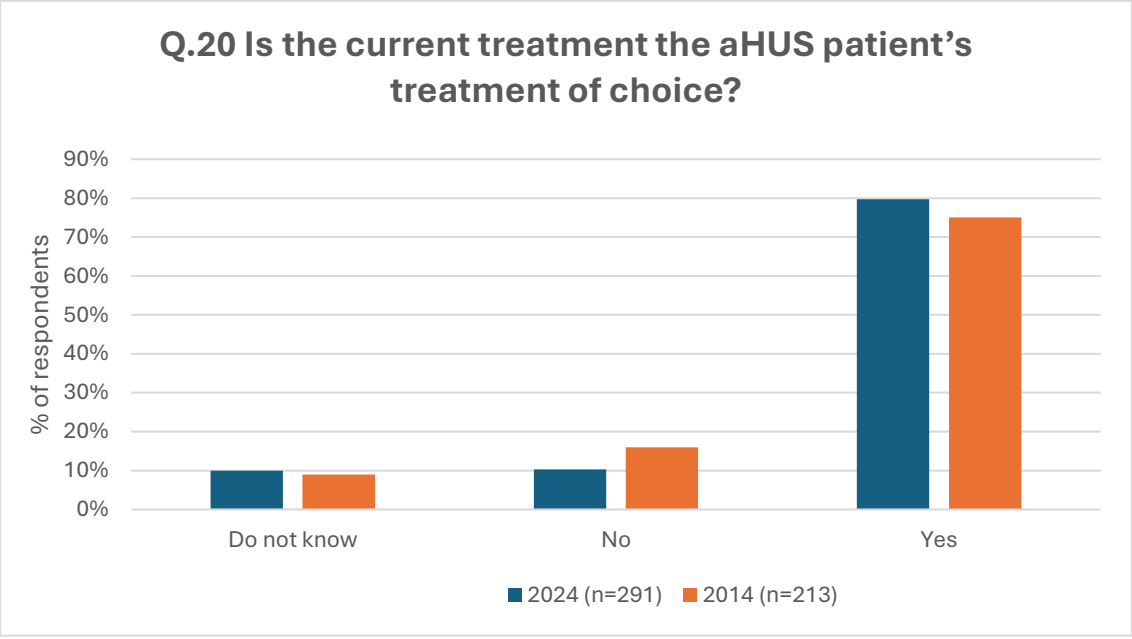
In 2014, a greater proportion of aHUS patients were on dialysis while awaiting a kidney transplant supported by a complement inhibitor, making this question particularly relevant to patient experience at that time. By 2024, the percentage of patients who had received a kidney transplant had increased significantly to 15%, up from 4% in 2014. Similarly, the use of dialysis declined:

- Peritoneal dialysis: 3% in 2024 (down from 5%)
- Haemodialysis: 14% in 2024 (down from 22%)

The proportion of patients who did not require renal replacement therapy remained stable at 68% in 2024 (compared with 69% in 2014).

Overall, the total proportion of patients receiving renal replacement therapy remained similar between the two surveys. However, there has been a clear shift away from dialysis towards kidney transplantation.

Figure 14. Is the current treatment the patient's treatment of choice?



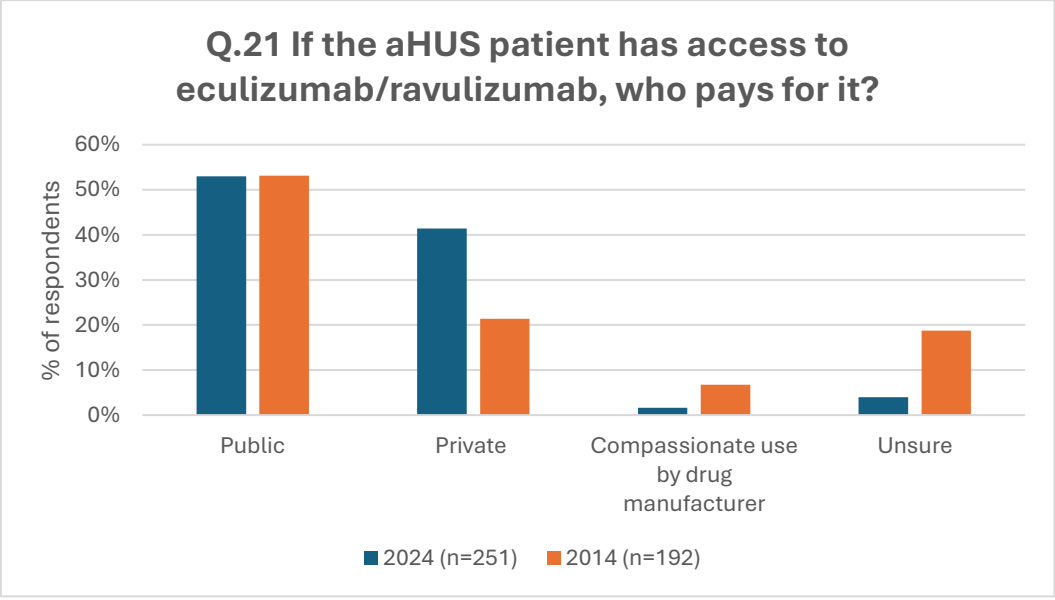
Patients naturally seek the least burdensome and most effective treatment available. In 2014, this meant opting for complement inhibitor therapy—despite requiring infusions every two weeks—rather than remaining on dialysis, even if it involved a kidney transplant.

By 2024, treatment options had expanded. Ravulizumab offered a more convenient eight-week dosing interval, whereas other emerging complement inhibitors included self-administered subcutaneous injections every four weeks or daily oral tablets. This made the question about whether patients were receiving their preferred treatment even more relevant.

Satisfaction with the current treatment increased: the percentage of participants who reported being on their chosen treatment increased from 75% in 2014 to 80% in 2024. The percentage of those who felt that they were not on their chosen treatment decreased from 16% to 10%, while the undecided group remained stable (10% in 2024 vs. 9% in 2014).

Overall, patient satisfaction with treatment improved between the two surveys. However, the availability of newer, less burdensome complement inhibitors had not yet produced a noticeable additional effect on treatment preference at the time of the 2024 survey.

Figure 15. If a patient has access to eculizumab/ravulizumab treatment, who pays for it?



Rare disease treatments are frequently very expensive. The annual cost of complement inhibitor treatment for adult patients is approximately $600,000 to $700,000 at the list price. Hospitals may also add their own markup.

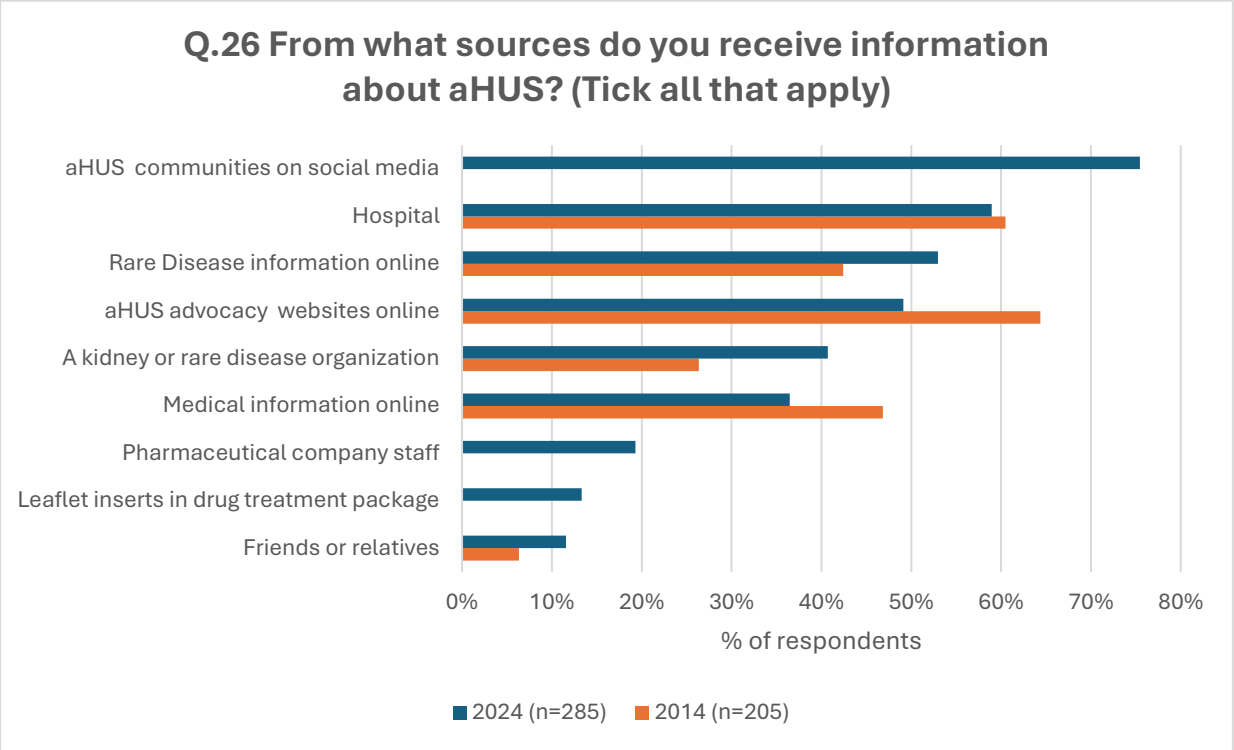
This section of the survey examined how patients fund their treatment. Funding certainty has improved markedly. In 2024, only 4% of participants were unsure about who paid for their treatment, which was a decrease from 19% in 2014. Public funds remained the largest single source of funding, stable at 53% in both survey years. However, the rate of private funding nearly doubled, rising from 21% in 2014 to 41% in 2024.

Overall, there has been a clear shift in how aHUS patients finance their high-cost complement inhibitor therapy. While public funding continues to play a dominant role, the substantial increase in private funding and greater certainty around payment sources suggest improved access to treatment and greater financial clarity for patients between 2014 and 2024.

Information and Support Experience

Soon after diagnosis, aHUS patients typically want to learn more about the disease and its treatment beyond the initial explanation provided by their healthcare professionals. In many cases, their families and caregivers begin seeking information even earlier, asking doctors and clinical teams what is happening and why.

Figure 16. aHUS information sources

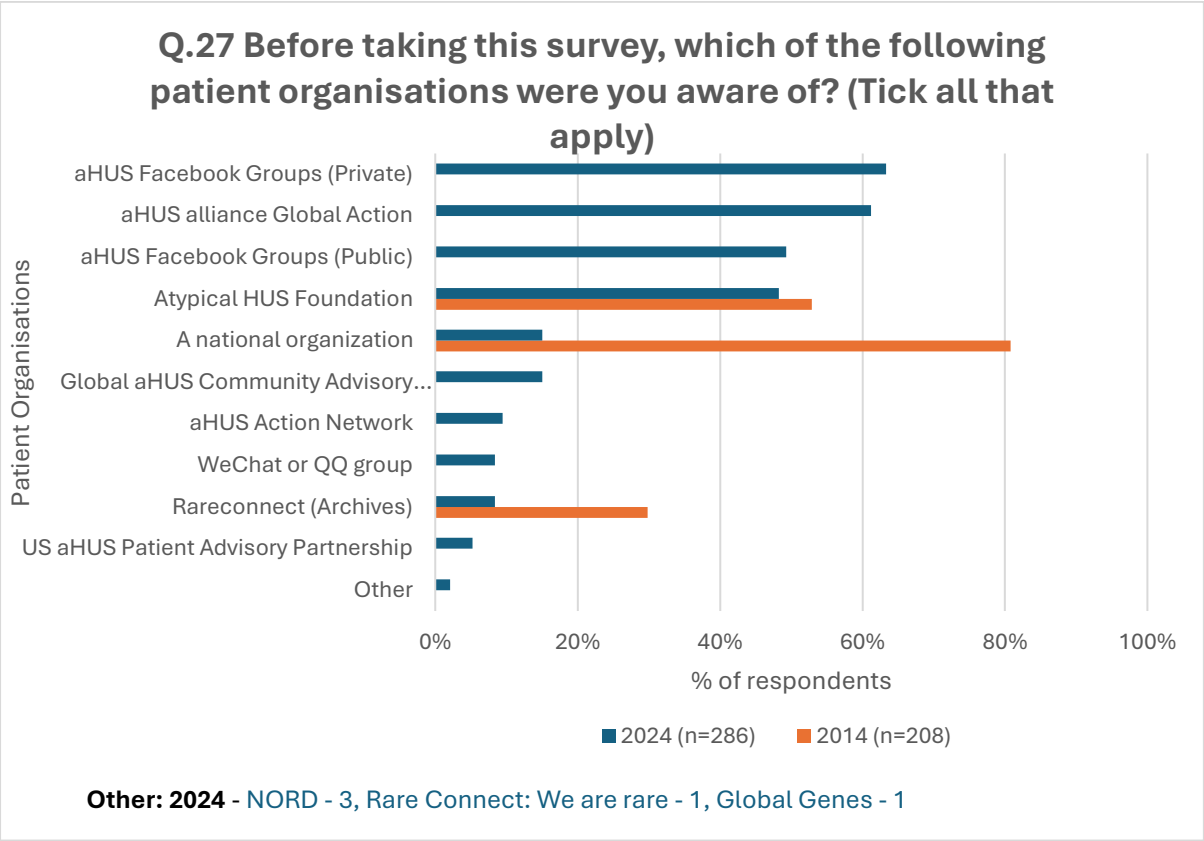


Over time, patients' search for information broadens as their experience with the disease evolves. This question explored not only the sources of aHUS information available to patients but also their preferred sources. Online aHUS-specific communities (e.g., Facebook groups) have become the most popular source of information, rising dramatically from 0% in 2014 to 75% in 2024. Other key sources in 2024 were as follows:

- Hospitals/clinicians: 59% (largely unchanged from 60% in 2014)
- Online rare disease organisations: 53% (up from 42%)
- aHUS-specific patient advocacy groups: 49% (down from 64%)
- Rare kidney disease organisations: 40% (up from 26%)
- Pharmaceutical company staff: 19% (up from 0%)
- Patient information leaflets (included with medicines): 13% (up from 0%)
- Friends or relatives: 12% (up from 6%)

Many sources of information are now available to aHUS patients, but the landscape has shifted significantly towards online resources. In particular, aHUS-specific patient communities have seen explosive growth in popularity and have become the leading source of information in 2024. This reflects the increasing value that patients place on peer support and real-world experience shared within the patient community.

Figure 17. Patient groups known to the respondents



aHUS-specific patient advocacy organisations aim to provide disease information support and disease awareness. In 2014, the aHUS alliance sought to determine which organisations, aHUS specific or otherwise, had raised awareness among aHUS patients.

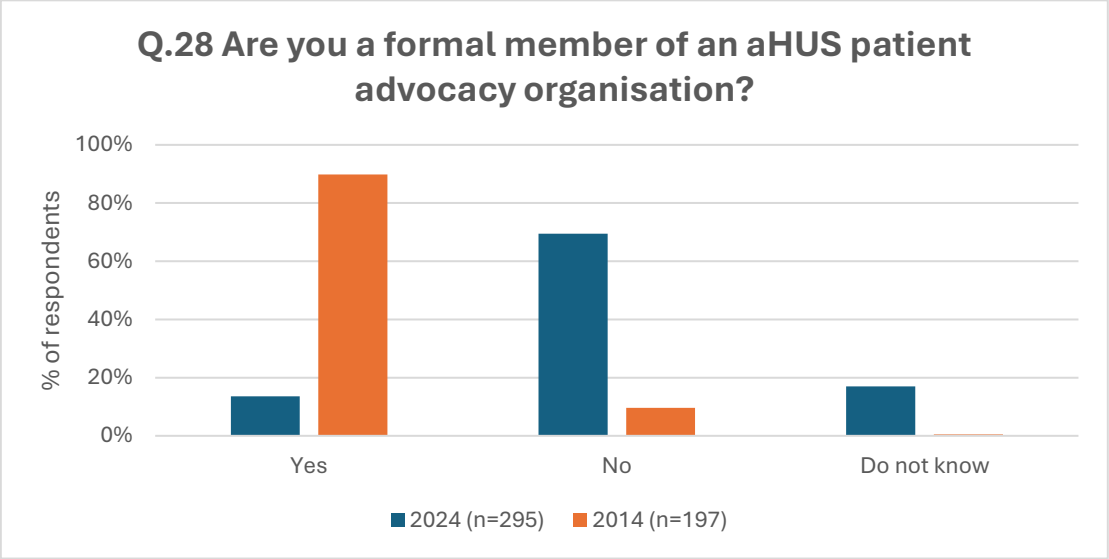
By 2024, three groups had emerged as the most widely recognised by patients. Awareness of Facebook groups (both private and public) increased dramatically from 0% recognition in 2014 to 63% (private) and 43% (public). The aHUS Alliance Global Action,

founded in 2016, also achieved strong recognition at 63%. The recognition of the other groups changed as follows:

- RareConnect (the original global platform): decreased sharply from 30% to 8%.
- National patient advocacy groups declined significantly from 80% to 15%.
- The Atypical HUS Foundation (USA) remained relatively stable at 48% (compared with 53% in 2014).
- Action Alliance Network (USA): 9%.
- USA Patient Advisory Partnership: 5%.
- Global aHUS Community Advisory Board (formed in 2023): 15%.
- WeChat and QQ Groups (China-only platforms): 2%.

The landscape of the aHUS patient community has undergone considerable changes over the past decade. There has been a clear shift towards global and social media-based groups, particularly Facebook communities and the aHUS Alliance Global Action, while the recognition of several established national and earlier global platforms has declined. This reflects evolving patient preferences for accessible, peer-driven, and internationally connected sources of support and information.

Figure 18. Is the respondent a formal member of an aHUS patient advocacy organisation?



Initial experiences with patient advocacy groups, whether formal or informal, are generally passive. Over time, however, many patients and caregivers become more active, with some progressing to formal membership and taking on roles in group management, decision-making, and long-term continuity.

In 2014, patient groups were focused on increasing their membership to strengthen advocacy efforts, such as campaigning for access to eculizumab in their countries. Since then, formal membership has declined sharply.

In 2014, 90% of participants regarded themselves as formal members of an aHUS patient advocacy organisation (Fig. 18) By 2024, this had decreased to 24%.

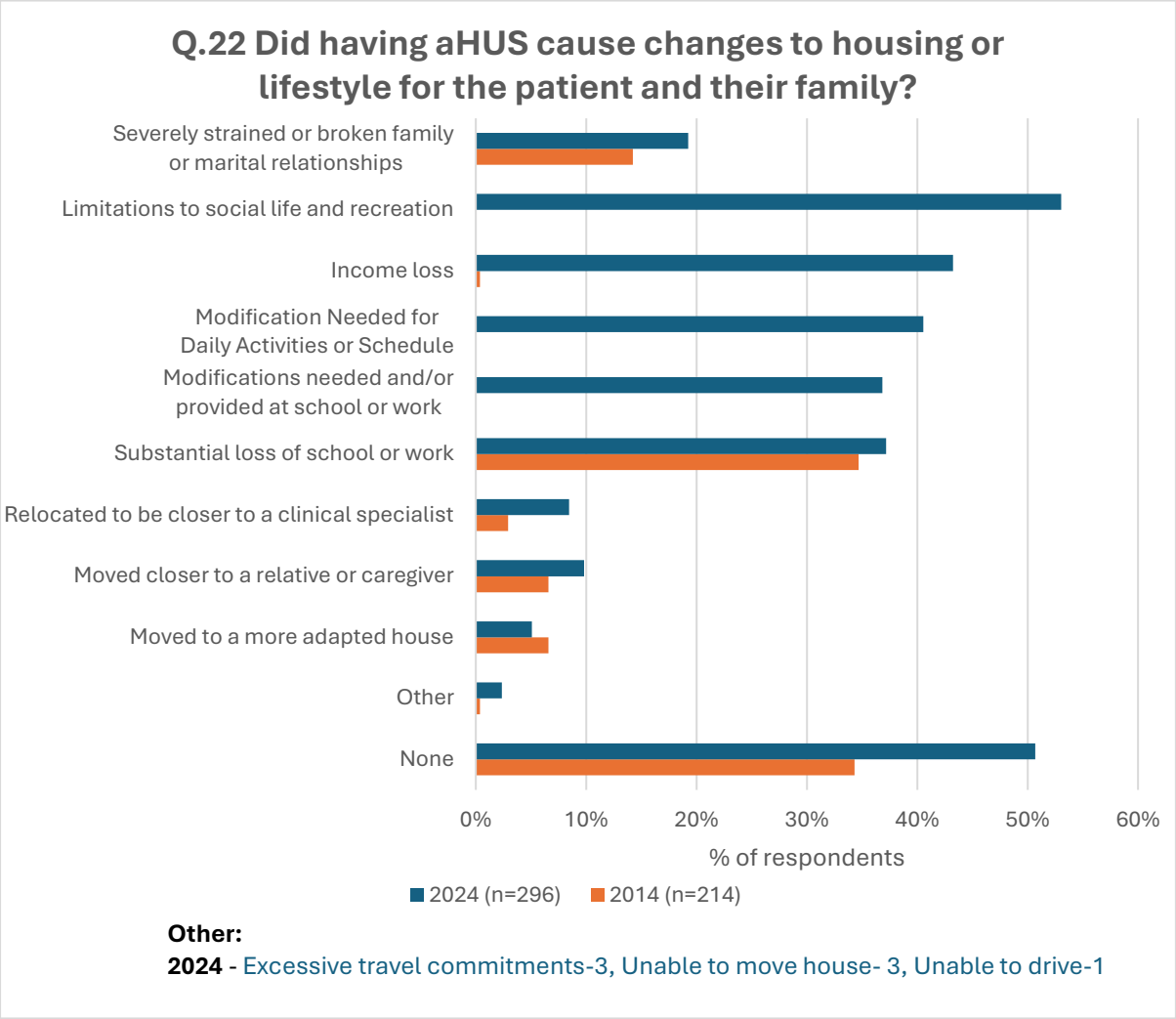
Conversely, the percentage of participants who were certain that they were not members of an organisation increased from 10% to 70% in 2024. A further 17% of patients in 2024 were unsure whether they were members (up from 0% in 2014).

There has been a significant decline in formal membership in aHUS patient advocacy organisations over the past decade. While patients and caregivers appear to value access to

information and peer support, they are now far less likely to become formal members than they were in 2014.

Societal Experience

Figure 19. Societal impact



In terms of whether a life-threatening acute episode occurs or disease progression is more gradual, rare disease patients and their caregivers often need to adjust where and how they live. This question explored the adjustments aHUS patients have made to live with their condition going forward.

In 2024, 51% of participants reported that no adjustments were needed, up from 34% in 2014 (Fig. 19). The remaining participants reported experiencing one or more impacts on their lives.

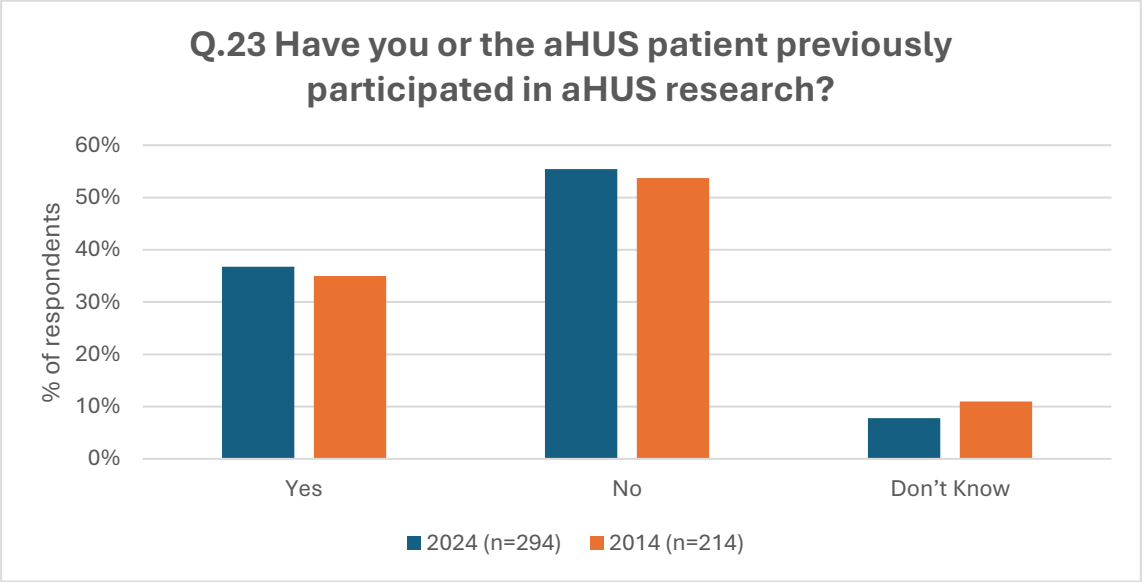
- Moving house or location:
  - To a more accessible/adapted home (e.g., for home haemodialysis): 5% (down from 7%)
  - To a location closer to family or caregivers: 10% (up from 7%)
  - To a location closer to a specialist aHUS centre: 8% (up from 3%)
- Education and employment:
  - Impact on school or work attendance: 37% (up from 0%)
  - Modifications needed by schools or employers: 43% (up from 0%)
- Financial impact: Increased loss of income: 43% (from 0% in 2014)
- Daily living: Modifications to daily activities or schedules: 41% (up from 0%)
- Social life and recreation: 53% (the most commonly reported impact, up from 0%)
- Family and relationships: Severely strained, broken, or affected marital/family relationships: 19% (up from 14%)

While just over half of the participants in 2024 reported needing no major adjustments to where they lived, a substantial proportion experienced significant changes in how they lived. The greatest impacts were seen in social life, daily routines, education/work, income loss and family relationships. These findings highlight the broad and ongoing effects of aHUS on patients' quality of life beyond purely clinical management.

Research Engagement Experience

Conducting research on rare diseases, their treatments, and patients' lived experiences is challenging. This section of the survey examined patients' and family members' willingness to participate in aHUS research, as well as their actual experience of engagement.

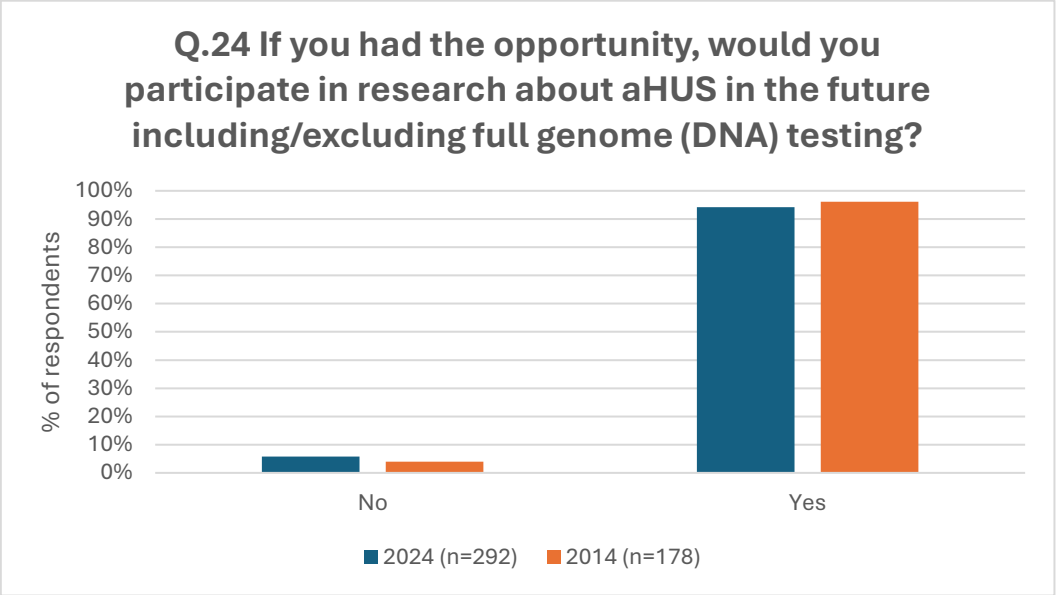
Figure 20. Has the patient or a family member participated in aHUS research?



Participation levels remained relatively stable between the two surveys. In 2024, 55% of participants reported no involvement in aHUS research, compared with 53% in 2014. The proportion of participants who had taken part in research was also similar: 37% in 2024 versus 35% in 2014. The number of respondents who did not know whether they or a family member had participated decreased slightly, from 12% in 2014 to 8% in 2024.

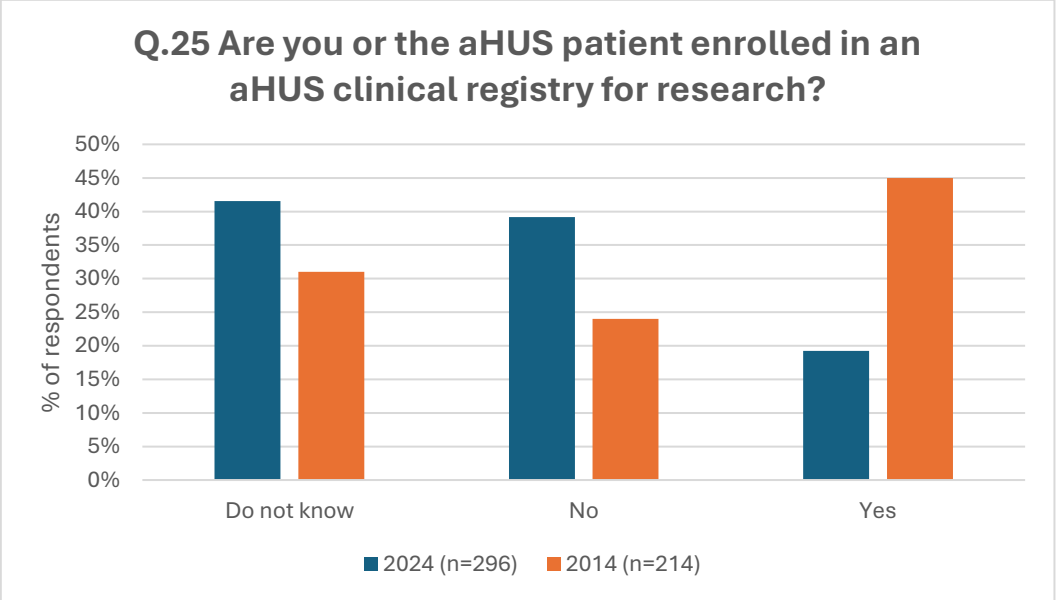
Overall, there has been little change in research participation rates over the decade. Just over one-third of the respondents reported involvement in aHUS research, while more than half had not participated. The modest reduction in uncertainty suggests improved awareness or communication about research opportunities.

Figure 21. Would the patient or family member participate in research in the future?



Willingness to participate in research is important for the recruitment of volunteers for a trial or study (including the use of personal medical records). A high proportion of participants in both years reported that they would participate in research (96% in 2024 compared with 94% previously) (Fig. 22), and there was a corresponding decrease in the percentage of participants who would not. There is a clear willingness from participants to be engaged by researchers to improve the patient experience of living with aHUS.

Figure 22. Is the patient enrolled in an aHUS registry?

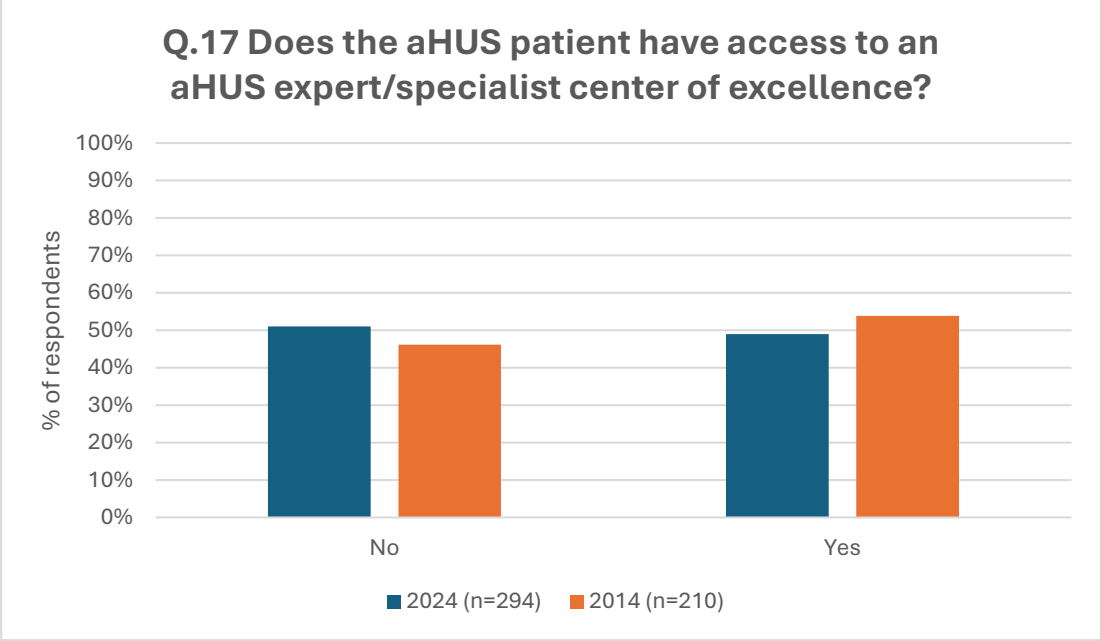


Patients can benefit from being included in an aHUS registry. These registries play important roles in the long-term monitoring of clinical and health outcomes, which can be reassuring for patients and families, sometimes many years after disease onset.

However, registry participation remains limited. In 2024, only 18% of participants reported being enrolled in a registry, down from 45% in 2014 (Fig. 22). Moreover, the percentage of patients who were uncertain about whether they were in a registry increased significantly to 43% (from 31% previously).

Few patients were certain that they were enrolled in an aHUS registry, and an increasing number of patients were certain that they were not. The high and rising level of uncertainty regarding registry participation is a notable finding that warrants attention and understanding from the aHUS community.

Figure 23. Does the patient have access to an aHUS specialist/expert centre?



Although there is no universal definition of an aHUS specialist or expert centre, these centres are typically recognised for their expertise in diagnosis, treatment advice to local clinicians, and a strong track record of published research. Patients often benefit from contact with knowledgeable experts and the opportunity to participate in research studies.

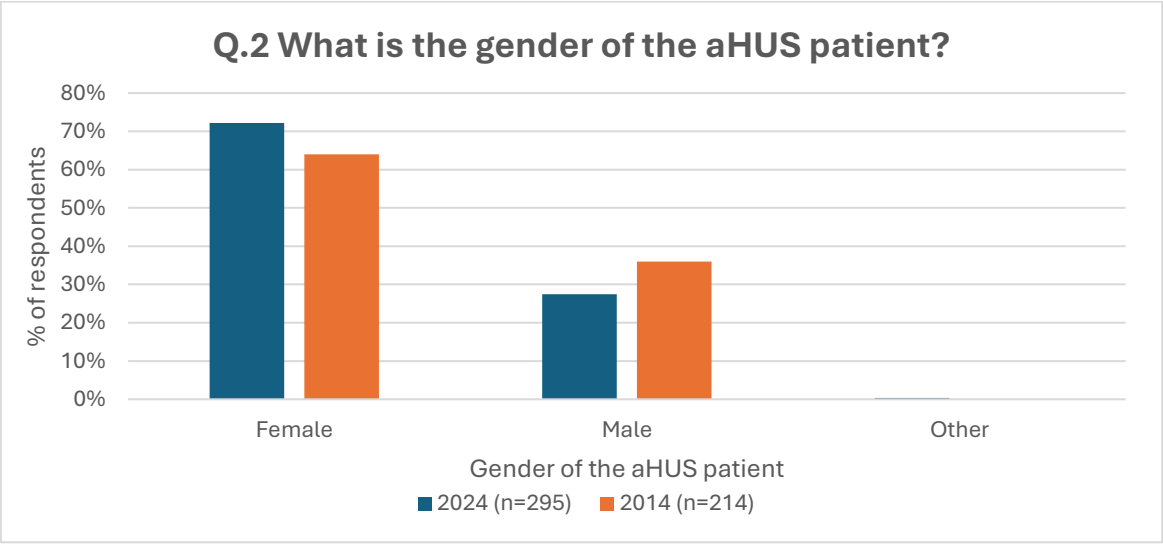
Access to these specialist centres has remained relatively stable but has slightly declined (Fig. 23). In 2024, 49% of participants reported having access (down from 54% in 2014), while the percentage without access increased to 51% (up from 46%).

Overall, access to aHUS specialist or expert centres remains limited to approximately half of patients. While the situation has been relatively consistent over the past decade, the slight downward trend highlights the need for continued efforts to improve equitable access to specialised care.

Patients Gender and Age Experience

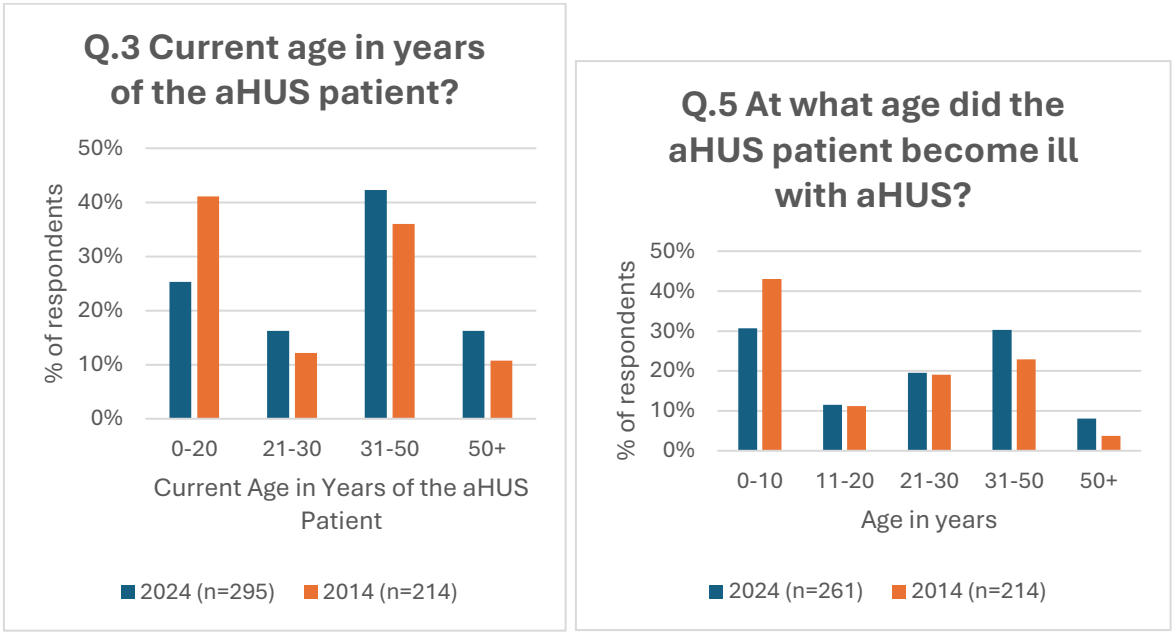
Rare diseases often affect females and younger individuals disproportionately. The inclusion of questions on gender and age in surveys helps clarify participant demographics and potential differences in disease experience.

Figure 24a. Gender



Rare diseases frequently affect more females than males, and this pattern was clearly evident in both the aHUS surveys. Females represented 64% of the participants in 2014, which is expected to increase to 72% by 2024. There were 36% and 28% males, respectively. These results confirm that aHUS is experienced predominantly by female patients.

Figure 24b. Age at onset and current age



These questions captured both the patient's age at disease onset and their age at the time of survey participation.

Age at Onset

- Under 21 years: Decreased from 56% in 2014 to 43% in 2024 (still the most common group)
- 21–30 years: Remained stable (19% in 2014 vs. 20% in 2024)
- 31–50 years: Increased from 22% to 30%
- 51+ years: increased from 4% to 8%

Overall, there was a relative shift towards a greater age at disease onset in 2024 than in 2014. The mean age was estimated to be 4.6 years older, which was based on the middle points of the age group (10.5, 25.5, 40.5 and 61.5*), and applying the reported percentages, there was an average of 22.1 years in 2014 that increased to 26.7 years in 2024.

*The 61+ group had an assumed midpoint of 72 years.

Current Age

- Under 21 years: Decreased significantly from 41% in 2014 to 26% in 2024

- 21–30 years: Increased from 12% to 16%
- 31–50 years: Remained the largest group, rising from 36% to 42%
- 51+ years: Increased from 11% to 16%

Overall, the current age profile of the aHUS patients who participated in the survey was older than it was in 2014. When estimated at an average of an additional 5 years, again selecting the age group middle points (10.5, 25.5, 40.5 and 61.5*) and applying reported percentages for the two years resulted in an average of 33.7 years in 2024 up from 28.7 years in 2014.

Therefore, the average patient experience of living with aHUS starts later and lasts longer.

Figure 25. Summary of key findings from the 2024 poll

Summary of key findings from the 2024 poll		
1 There has been an increase in patients having tests for TTP and HUS.		**12. aHUS-specific online patient communities have seen explosive growth in popularity and have become the leading source of information by 2024.**
2 There has been an increase in the number of patients initially misdiagnosed with TTP or HUS.		**13. Patient and caregivers prefer accessible, peer-driven, and internationally connected sources of aHUS support and information.**
3 **The diagnostic timeline has improved from an average of 132 days in 2014 to 87 days in 2024.**		**14. Half of patients have needed no adjustments to live with aHUS.**
4 **The majority of patients are still diagnosed with one or two doctors. There has been a clear shift over the ten-year period towards greater involvement of multiple specialists and multidisciplinary teams.**		**15. The greatest societal impacts were found in social life, daily routines, education/work, income loss and family relationships.**
5 Although it was found that 14 medical specialists can be involved in an aHUS diagnosis and management nephrologists, haematologists, and paediatricians remain the core specialists.		**16 Only a third of patients have been engaged in aHUS research.**
6 There has been a clear improvement in turnaround times for genetic test results.		**17 Patients and caregivers are overwhelmingly willing to volunteer for aHUS research.**
7 Access to genetic testing has not increased over the period and remains just below 90%.		**18 Patents are uncertain if they are in aHUS registries.**
8. Complement inhibitor use has risen substantially over the past decade, with a		**19 Access to specialist/expert centres limited to half of patients.**

noticeable switch from eculizumab to ravulizumab.		
9 There has been a clear shift away from dialysis towards kidney transplantation.		**20 More females have aHUS than males.**
10 Patients satisfaction with their treatment improved between the two surveys. By 2024 potential newer less burdensome complement inhibitors had not affected patient preferences.		**21 On average, patients are experiencing first aHUS onset at 27 years old, 5 years later than in 2014.**
11 While public funding continues to play a dominant role in the payment for complement inhibitor treatment, there has been a substantial increase in private funding.		**22. Patients are living longer.**

Discussion

The purpose of the 2024 poll was to compare and contrast the lived experience of aHUS patients with that of a previous poll in 2014. The key findings from the results of the survey are shown in Fig. 25.

Diagnosis Experience

Usually, patients' first experience of aHUS is that of a medical emergency, which is difficult for their doctor to explain and treat [4]. From the outset, what happens will determine their future lived experience [42]. Once a TMA is identified, a diagnosis of exclusion begins, and aHUS is usually suspected only after all other TMAs are discounted [43]. Several models for TMAs in children, adults and pregnant patients are available for doctors if they are aware of them [45–47]. The first two TMAs to be excluded are TTP and HUS, as they have reliable, specific and sensitive diagnostic tests [48].

Our survey revealed that not all patients were tested for HUS/TTP and that 30% were misdiagnosed with TTP or HUS. In critical and grave circumstances, communications between doctors and caregivers may not be as clear as it could be, and misunderstandings may arise; however, doctors have been known to interpret ADAMTS13 test levels above the diagnostic 5 to 10% test threshold criteria as an "idiopathic" manifestation of TTP rather than

suspect aHUS [49]. Approximately 15% of aHUS patients have a family history of aHUS, which, if known, may have guided their doctor and not necessitated any tests [50].

While we found that on average, an aHUS diagnosis in 2024 took 45 days less than in 2014, the average time taken was 87 days. There is room for improvement, particularly given that 40% of patients reported receiving a diagnosis within 7 days, a level that ensures the best health outcomes for patients living with aHUS [21]. Coordinated research similar to that on other diseases could examine the extent and reasons for aHUS diagnosis delay or error, which could improve medical practice in reducing TMA diagnosis timelines [51]. A formal multidisciplinary team approach could also assist [52–55] because, depending on aHUS triggering conditions, as many as 14 different medical specialists can be involved in making a diagnosis. Furthermore, medical training syllabi for TMAs should be expanded to improve recognition of medical emergencies among general practitioners [56].

Although a complement genetic test result is not necessary for initiating treatment for a patient with suspected aHUS, we found that access to these tests still falls short of 100%. Although the estimated average turnaround time (derived from the midpoints of the time taken bands and percentage of participants reporting each band) was 45 days shorter in 2024, i.e., between 135 and 98 days, these turnaround times should be closer to a 7-day target for diagnosis. The results needed to counsel family members are not needed as urgently. Across rare diseases, the principal value of genetic testing often extends beyond diagnosis, providing critical information for prognosis, treatment selection, disease monitoring, recurrence risk assessment, and genetic counselling. Nevertheless, the reporting quality should not be reduced to increase the reporting speed or simplicity and meaningfulness to patients [57].

Treatment Experience

The best treatment for aHUS in the acute phase, and when needed thereafter, is a complement inhibitor [58]. In the event of disease progression to end-stage kidney disease, a

kidney transplant, with or without ongoing complement inhibitor therapy, is superior to dialysis as a form of renal replacement therapy [59].

Our survey revealed that complement inhibitor use has increased significantly because of improved access. Most patients are now receiving the longer-acting modified version of eculizumab (Soliris [60]), known as ravulizumab (Ultomiris) [61]. The greater participation of patients in the USA in the survey is likely to have influenced these findings (Fig. 1b). The shift away from long-term dialysis towards kidney transplantation also reflects better access to complement inhibitors

The proportion of patients in untreated remission has decreased. aHUS generally enters remission only after significant kidney damage has occurred, and more dialysis patients were in remission in 2014 [59]. aHUS can reoccur after a transplant and complement inhibitors are used [62]. Vials of eculizumab and ravulizumab are expensive, and the number needed at standard dose intervals throughout a single year can result in a treatment cost for an adult between $600,000 and $700,000 [63]. Complement inhibitors continue to present a major funding challenge. This requires higher private insurance reimbursement in some cases and places a substantial burden on government healthcare budgets in others. Our findings may not fully capture the scale of emerging treatment discontinuation strategies [64] aimed at reducing overall costs [65]. Any discontinuation must be undertaken in a carefully considered and safe manner, with patients actively involved in the decision-making process [66]. The risk of relapse off treatment must be mitigated through rapid reinitiation of therapy if relapse occurs to prevent irreversible harm [66].

With access to complement inhibitor options and supported kidney transplants, patient satisfaction with treatment is high. However, other treatment options are in development, which could rival the clinical effectiveness of current complement inhibitors and may be less burdensome to administer than the current infusion process is. Crovalimab is a self-

746 subcutaneous injection [67], and iptacopan is a twice-daily oral pill [68, 69]. Patient
747 satisfaction and preferences could differ, but more research is needed to determine what
748 matters to patients in choosing their most personalised treatment if clinical effectiveness is
749 equal.

750 ***Information and Support***

751 Individuals living with rare diseases, including aHUS, frequently experience feelings
752 of isolation and struggle to find reliable information about their condition, even from
753 healthcare professionals [70, 71]. Only 60% of the participants with aHUS considered their
754 hospital or clinicians as trusted sources of information (Fig. 16). These findings align with
755 broader evidence showing that many clinicians perceive their own knowledge of rare diseases
756 as insufficient or very poor, with few feeling adequately prepared to care for patients with
757 these conditions [72]. Often, the experience of aHUS patients given anecdotally is that their
758 healthcare professionals need them to explain their disease and treatment, which adds to a
759 loss of confidence and the need to seek alternative sources.

760 Once the preferred source, dedicated aHUS advocacy websites and general online
761 medical searches have declined. Over the past ten years, aHUS communities on social media
762 platforms have emerged as the most frequently used sources, not only for information but
763 also for mutual support between peers. However, if unmoderated, there is evidence of
764 widespread misinformation, e.g., on treatment, diseases and vaccinations, creating risks of
765 poor decision-making [73–75].

766 aHUS patient organisations play a role in influencing health policies and care, which
767 can improve the experience of living with the disease [76] by helping policy makers
768 understand their lived experience [77].

769 Although North America–specific programmes such as Alexion Pharmaceuticals'
770 OneSource™ are inherently product focused, they provide education,

771 insurance/reimbursement navigation, access assistance and copay connections [78].
772 Elsewhere in the world, direct assistance by Pharma is not permitted under Pharma/Patient
773 regulations or is not needed because of social funding of treatment. Any aHUS patient
774 education programmes for patients are funded by unrestricted educational grants but
775 delivered by third-party organisations such as the National Renal Complement Therapeutics
776 Centre (NRCTC) in the UK [79].
777 Pharmaceutical companies are obligated to produce patient information leaflets (PILs)
778 that answer all the questions about the use of a drug, including dosing levels, precautions and
779 side effects. These are provided with every vial carton [80]; however, our survey reveals that
780 their use is low because of a lack of awareness, and the leaflet is usually disposed of with the
781 vial carton in medical waste. This is not unusual for all PILs [81], even though efforts are
782 made to make them comprehensible and user friendly [82]. However, under the Risk
783 Evaluation and Mitigation Strategy (REMS) in the USA and Risk Management Plan (RMP)
784 and Additional Risk Minimisation Measures (aRMMs) in the EU, doctors are required to
785 provide the leaflet/guide and other educational material to the patient [83, 84]. Therefore, on
786 the first occasion of receiving treatment, it would be reasonable for healthcare professionals
787 to pass a copy from one of the vial cartons to the patient or caregiver. These would answer
788 many of the initial questions about the disease and its treatment and help those new to the
789 experience of living with aHUS.

790 ***Societal Experience***

791 The impact of societal factors on people with rare diseases can affect their day-to-day
792 lives [85], including what they can do and where they live. We found (Fig. 19) that the
793 awareness of societal factors had risen by 2024 when patients surveyed in 2014 reported that
794 this was not their primary experience or concern. However, in 2024, approximately just over
795 half of aHUS patients reported no societal impact from having aHUS. Those who did report

some listed far more lifestyle challenges than housing-related ones. This could be seen as a patient benefit arising from the reduced need for home adaptations for home kidney dialysis [86, 87].

Nevertheless, concerns remain about interruptions to education and employment, despite a reduced treatment burden (moving away from dialysis) and the switch from eculizumab's two-week dosing interval to ravulizumab's eight-week cycle. More needs to be known about the long-term effects of lost education and/or employment, as well as income loss, disruptions to and restrictions on daily routines and recreation, the fracturing of family relationships, and the interventions needed [3].

Research Engagement Experience

While research and registries might not appear to directly impact the day-to-day experience of people living with aHUS, participation in research and registries can be beneficial to their own and others' future experience of living with the condition. In particular, patients reported outcomes and possible interventions to mitigate them [3]. Research on rare diseases is challenging [88], and few disease-specific registries exist [89–91]. Our findings (Fig. 19) show that patients have a favourable research experience, given their willingness to participate again, together with a similar willingness among those who had not yet participated in any aHUS research or registry. However, in practice, there may be limitations to long-term commitment to important trial/study follow-up and feedback [92]. Better communication with participants would help retention, particularly regarding the impact on the patient's lived experience [93]. Continental network hubs such as the European Reference Network for Rare Kidney Diseases (ERKNet) and the USTMA Consortium Alliance could improve volunteer recruitment, especially for trials for new therapies [41, 94].

Gender and Age Experience

Our findings support the idea that aHUS is largely experienced by female patients (Fig. 24a). The reported global age range is approximately two female patients for every male [94–99]. We reported that 18% of the disease triggers (Fig. 9) were reproduction related. Postpuberty is usually the time period when the condition is found to shift from a gender-neutral experience to a female experience [100]. It is common for most rare diseases to impact females [101]. More understanding is needed of why this is the case in aHUS and whether there is any hormonal impact on complement activation and any gender-based differential prognosis.

Our findings also support that aHUS can be experienced for the first time at any age (Fig. 24b). This is different from rare diseases, where as many as 70% of cases manifest in childhood [102]. Global aHUS studies in all ages usually reveal more adult patients than children [17]. Our estimates of the duration lived with aHUS after onset show that in 2024, aHUS patients are on average living five years longer than they were ten years before, which is a very important finding concerning the experience of living with aHUS.

Limitations of our Survey

Recognising the retrospective nature of most items, which rely on the recall of events and subjective experiences, potential recall bias is acknowledged. Such bias may lead to underreporting of events or inaccuracies in timelines [103, 104].

Although the survey responses were from random participants, the reach may have been limited because of the communication platforms deployed despite the use of different language questionnaires. The experience of patients in the USA (Fig. 1b) is overrepresented and could therefore reflect a more advanced medical environment that impacts the experience of living with the disease.

The loss of data due to the dissolution of RareConnect made it impossible to conduct an in-depth analysis to correlate and compare the underlying explanatory evidence.

Conclusion

In this unique opportunity to survey patients' experiences of having and living with aHUS through two surveys conducted ten years apart, we have found meaningful progress in access to complement inhibitor treatment. We found that patients are living longer and confirmed that the experience is predominantly faced by females. However, significant challenges remain; in particular, further efforts are needed to achieve a rapid aHUS diagnosis to ensure the best health outcomes and improve quality of life. We also reported that new communication technologies have developed and could be further developed to empower patients to manage their condition and improve their experience. Surveys have shown that only half of patients experience some societal impact, and more needs to be done to understand the long-term consequences, particularly of lost education and employment, in those who experience them. Although it does not impact day-to-day lived experience, greater participation in research, registries and expert centres could improve future patient experience. Regular tracking of patient experience is essential to help achieve optimal health outcomes and quality of life for those living with aHUS.

Declarations

Ethical Approval

This study involved an anonymous noninterventional online questionnaire about lived experience with minimal risk to participants. Ethical approval or waiver were not required. Participation was voluntary, and informed consent was explicit.

Consent for Publication

No individual identifying data are included. Participants confirmed their informed consent prior to completing the questionnaire.

Availability of Data and Materials

The participant were informed that the data will not be shared with third parties.

Competing Interests

LB and KS are members of the aHUS Global Community Advisory Board, which receives honoraria and disburses expenses on their behalf from Astra Zeneca, Roche Pharmaceuticals and Novartis. LW has no competing interest to declare.

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Authors' Contributions

LW and LB conceived the study. LW, LB and KS designed the survey questionnaire, and KS and LW facilitated its translation. KS set up the questionnaire online and consolidated the data. LW and LB analysed the results. LW, LB, and KS wrote the manuscript. LW, LB and KS approved the final draft.

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APPENDIX A

2024 Global Poll Questionnaire

1. The **person** filling in the questionnaire is …

2. What is the gender of the **aHUS patient**?

3. What is the current age of the **aHUS patient**?

4. What is the **aHUS patient's** country of residence?

5. At what age did the aHUS patient become ill with aHUS?

6. Has the **aHUS patient** undergone genetic screening for aHUS?

7. The results of this question are not included in this article.

8. If genetically screened, how long did it take for **you** to receive results?

9. What do **you** assume was the likely trigger of the first manifestation of aHUS in the patient?

10. Was the **aHUS patient** initially diagnosed with TTP or HUS?

11. Did the **aHUS patient** receive an ADAMTS13 or *E. coli*/Shiga toxin test?

12. How long did it take for the **aHUS patient** to be correctly diagnosed with aHUS?

13. How many doctors did the **aHUS patient** see before an accurate diagnosis was made?

14. What specialists were involved in the **aHUS patient's** diagnosis?

15. At any time in the years before becoming ill with aHUS (including childhood), did the **aHUS patient** experience any of the following unexplained symptoms?

16. If the **aHUS patient** experienced misdiagnosis or delay or lack of diagnosis, were there any medical consequences?

17. Does the **aHUS patient** have access to an expert/specialist centre of excellence?

18. What is the **aHUS patient's** current aHUS treatment?

19. Is the **aHUS patient** receiving any of the following renal replacement therapies?

20. Is the current treatment the **aHUS patient's** treatment of choice?

21. If the **aHUS patient** has access to eculizumab/ravulizumab, who pays for it?

22. Did having aHUS cause changes to housing or lifestyle for the **patient** and their **family**?

23. Have **you** or the **aHUS patient** previously participated in aHUS research?

24. If **you** had the opportunity, would **you** participate in research about aHUS in the future, including/excluding full-genome (DNA) testing?

25. Are **you** or the **aHUS patient** enrolled in an aHUS clinical registry for research?

26. From what source do **you** receive information about aHUS?

27. Prior to taking this survey, which of the following patient organisations were **you** aware?

28. Are **you** a formal member of an aHUS patient advocacy organisation?

Glossary of common aHUS terms

ADAMTS13 – A Disintegrin And Metalloproteinase with a ThromboSpondin type 1 motif, member 13

An enzyme that cleaves von Willebrand factor; activity <10% is diagnostic of TTP.

aHUS – Atypical haemolytic uraemic syndrome

A complement-mediated form of thrombotic microangiopathy characterised by microangiopathic haemolytic anaemia, thrombocytopenia, and acute kidney injury.

Anti-CFH antibodies – Autoantibodies against Complement Factor H

A common cause of aHUS in children (especially in certain populations).

C3/C5 – Complement component 3/Complement component 5

Key proteins in the complement cascade; C5 is the target of terminal complement inhibitors (eculizumab and ravulizumab).

C5 inhibitors – Terminal complement inhibitors

Monoclonal antibodies (eculizumab and ravulizumab) that block the cleavage of C5 and prevent the formation of the membrane attack complex (MAC).

CFH – Complement Factor H

A major regulatory protein of the alternative complement pathway; mutations or autoantibodies against CFH are common in aHUS.

CFI – Complement Factor I

A serine protease that inactivates C3b; genetic variants are associated with aHUS.

cTMA/CM-TMA – Complement-mediated thrombotic microangiopathy

The preferred modern term for aHUS when the disease is driven by complement dysregulation.

DGKE- Diacylglycerol Kinase Epsilon

Gene whose recessive mutations cause an early-onset form of aHUS that usually responds poorly to complement inhibitors

Diagnosis of exclusion

aHUS/cTMA is diagnosed after ruling out TTP (ADAMTS13), STEC-HUS, and secondary causes of TMA.

MAHA – Microangiopathic haemolytic anaemia

Fragmentation of red blood cells (schistocytes) due to mechanical damage to small vessels.

MCP/CD46 – Membrane Cofactor Protein

Cell-surface complement regulator; mutations are frequently linked to aHUS, especially childhood onset aHUS.

PE/PEX/TPE – Plasma exchange/Therapeutic plasma exchange

Historical first-line treatment for aHUS and TTP before complement inhibitors.

sC5b-9/TCC – Soluble C5b-9/Terminal complement complex

A marker of terminal complement activation that is sometimes measured in research or specialised centres.

Secondary TMA

Thrombotic microangiopathy caused by an underlying condition or trigger (e.g., drugs, malignancy, autoimmune disease, transplant, pregnancy, or severe hypertension) rather than primary complement dysregulation or ADAMTS13 deficiency.

STEC-HUS – Shiga toxin-producing *Escherichia coli*-associated haemolytic uraemic syndrome

Typical (diarrhoea-positive) HUS caused by Shiga toxin.

THBD – Thrombomodulin

An endothelial protein involved in coagulation and complement regulation; variants can predispose patients to aHUS.

TMA – Thrombotic microangiopathy

Pathologic process of microvascular thrombosis that leads to MAHA, thrombocytopenia, and organ injury (most often kidney injury).

Trigger

A clinical event (infection, pregnancy, surgery, drug use, etc.) that can precipitate an acute episode of aHUS in genetically predisposed individuals.

TTP – Thrombotic thrombocytopenic purpura

TMA caused by severe ADAMTS13 deficiency (<10%).

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