Meeting the ambitions of the UK's Rare Diseases Framework: Insights from the Gold Standard National Paroxysmal Nocturnal Haemoglobinuria (PNH) Service

A Case Study on the National PNH Service

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Introduction

The 2021 UK Rare Diseases Framework set out a clear ambition for improving the lives of people living with rare diseases, and the subsequent Actions Plans from England, Wales, Scotland, and Northern Ireland have outlined the practical steps that need to be delivered to make this a reality.

Paroxysmal nocturnal haemoglobinuria (PNH) is an example of one such rare disease for which the Framework and Action Plans are seeking to ensure that patients can receive the best possible care and treatment. However, PNH is an unusual and interesting case. Unlike many other rare diseases, there was already a world-leading and gold standard specialised service in place before the publication of the Framework. This 'PNH National Service' – established in 2009 – continues to grow and provide exceptional care today. Not only do the leaders from this service share their expertise throughout the UK, but they are also helping to further the knowledge of the PNH community around the world to drive much needed improvement in patient outcomes.

This report therefore examines the current policy environment for rare diseases in the UK and the vision for the future diagnosis, care, and management of these conditions – essentially what 'good' should look like by the end of the Rare Diseases Framework's lifespan in January 2026. Alongside this, it provides an overview of PNH and its impact on patients, and background to the PNH National Service itself. Finally, it considers how the UK's PNH National Service provides a case study in best practice for rare diseases in how to work towards achieving the goals set out in the Rare Diseases Framework, both in terms of the priority areas outlined for action and the underpinning themes. It notes where there have been significant successes as well as where lessons can be learnt for other rare conditions and is based on the insights that we have gathered from engagement with staff from within the PNH National Service.

Summary of Findings

Priorities from the Rare Diseases Framework		PNH National Service Provision
Priority 1: Helping patients get a final diagnosis faster	Getting the right diagnosis is key to effective management of rare disease, however, it has been consistently highlighted as one of the most significant challenges faced by the rare disease community.	Through extensive and targeted work with haematologists, the National PNH Service has supported greater awareness of PNH, aiding clinicians to consider the condition as part of early investigations and thus driving improvements to the time taken between a first referral and receipt of a final diagnosis. Upon diagnosis following a PNH cytometry test, there is rapid referral into the National PNH Service. The Service then triages patients based on level of clone and severity of symptoms, Patients are booked to earliest available clinic, with urgent patients seen within a few days.
Priority 2: Increasing awareness of rare diseases among healthcare professionals	It is important that healthcare professionals are aware of rare diseases more widely, alert to considering them, and are provided with the education and resources that can help them recognise rare diseases in patients and be aware of potential specialist treatment needs.	Through centralised efforts of clinical experts in PNH, education and awareness raising initiatives have been taken forward in a focused and effective way, to raise awareness of PNH as a condition. This includes the National PNH Service ensuring the availability of its expert team to participate in direct education initiatives, such as seminars in hospitals around the UK. The National PNH Service has also engaged with key clinical specialties beyond haematology, including urologists, hepatologists, gastroenterologists, and neurologists, all of which can play a role in the initial diagnosis of a PNH patient. At both a national and international level, the healthcare professionals working in the PNH service are recognised for their expertise, with the service ensuring it has a presence and is contributing at conferences around the world to support awareness of PNH.
Priority 3: Better co-ordination of care	Coordination of care is essential to ensure care is effectively managed, the burden on patients and their carers is minimised, and healthcare professionals are working together	Treatment for PNH patients is initiated by the PNH Service, with patients having extensive access to consultant time at first consultation. Weekly MDT meetings take place at Leeds and Kings, and monthly MDTs are carried out between the Kings

	to provide the best possible joined up and high-quality care.	and Leeds teams to assess patients on an ongoing basis. Care is co-ordinated to ensure patients can receive monitoring and treatment close to home wherever possible. The implementation of shared care agreements between the PNH Service and local hospitals ensures experts working in the service have oversight of patient care and can direct care, closely monitoring patients without them having to travel to the National PNH Service as frequently. In addition, the National PNH Service provides a 24/7 emergency line and on call service, which enables patients to have a specialist involved in any other aspect of their health care (for example an emergency presentation in hospital. The service also offers aplastic anaemia advice. Specialist nurses play a critical role in co-ordinating wrap around care, such as mental health support, alongside the administration of home care for treatment. The small, expert team of clinicians working within the National PNH Service ensures that all patients have a high level of consistency in who delivers their care, to support effective co-ordination around any health need.
Priority 4: Improving access to specialist care, treatments, and drugs	Patients need to have access to expertise in the treatment and care of their rare disease where available, and there are opportunities to develop innovative models of care across the healthcare system so that patients have their care delivered as locally as possible.	The National PNH Service is a beacon of excellence in relation to supporting clinical research, with clinical trials being a priority across the service. The high number of patients enrolled on clinical trials at any one time is a testament to the ethos within the service that seeks to ensure that all patients are offered the opportunity to participate in a trial. The availability of clinical experts working closely with patient support groups is a key element to supporting shared decision making and empowering patients around care and treatment options. As a result, PNH patients are often highly engaged in their care.

Overview of the Rare Diseases Framework

Rare disease in the UK

While rare diseases, by definition, are individually uncommon, collectively they are not. A rare disease is a condition that affects fewer than 5 in 10,000 in the general population,[1] and around 1 in 17 people will experience rare disease at some point in their lifetime.[2] At present, approximately 3.5 million people in the UK are living with one of over 7,000 rare diseases[1] - more than the population of Birmingham, Liverpool, Nottingham and Sheffield combined.[2]

Owing to their rarity, people living with rare diseases face a variety of challenges beyond those caused directly by their condition. They often face difficulties in receiving a diagnosis, which can delay timely treatment and affect patient outcomes. A lack of awareness of their disease outside of specialist services can impact care delivery, as well as their work, education, and/or social lives. Small patient populations can mean difficulties in recruiting for clinical trials,[3] which can also impact the evaluation of and access to medicines for rare diseases.

With this in mind, the UK Rare Diseases Framework was established to address the various challenges that people living with rare disease face, as the key policy driving rare disease strategy across all four nations in the UK.

Background to UK rare disease policy

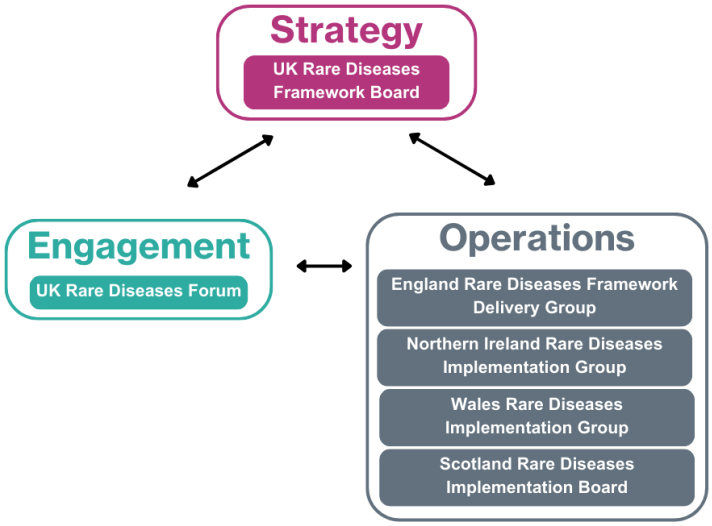
The 2021 UK Rare Diseases Framework[4] and its supporting national Action Plans are best understood in the context of the policy developments of the preceding decade. In 2009, an EU Council Recommendation[5] mandated each European Union member state to develop a rare disease plan by 2013. The resulting 2013 UK Strategy for Rare Diseases[6] was the first national strategy of its kind in the UK. Comprising 51 commitments designed to improve outcomes for patients, this set out actions in five key areas: patient empowerment; identification and prevention; diagnosis and early intervention; coordination of care; and research.[6]

Despite the ambitions of the Strategy being welcomed, it was criticised by many in the rare disease community for its lack of focus on implementation. The 2017 *Leaving No One Behind* report by Rare Disease UK for the All-Party Parliamentary Group (APPG) on Rare, Genetic, and Undiagnosed Conditions[7] highlighted that the NHS did not have the remit or capacity to influence the 51 commitments in the Strategy – and that despite the commitments, care continued to be poorly coordinated. There was also criticism of the pace of publication of each of the national action plans setting out how the Strategy would be implemented. Noting the Strategy's deadline for plans to be published by February 2014, the Implementation Plan for Rare Diseases in Scotland[8] was the first to be launched in July 2014, followed by its Welsh[9] and Northern Irish[10] counterparts in February and October 2015 respectively. The Implementation Plan for England[11] was not published until 2018 - five years after the Strategy - leading to considerable variation in how the four nations progressed against these commitments in this time.

The NHS Long Term Plan,[12] published in January 2019, also failed to address the breadth of issues faced by the rare disease community, mentioning rare disease under only one action on whole genome sequencing. This meant that non-genetic rare diseases were neglected entirely. Overall, this resulted in a pressing need to review the national rare disease policy landscape to prevent further fragmentation across the four nations.

With this in mind, the Government launched the National Conversation on Rare Diseases Survey in October 2019.[4] This comprised of a national consultation to seek the views of the patient community, researchers, and clinicians to understand the main challenges for those living and working with rare diseases. The input received was used to draft the priorities and underpinning themes of the UK Rare Diseases Framework, which were tested through direct stakeholder engagement with patient representatives, clinicians, researchers, and industry representatives, before being put to the UK Rare Disease Policy Board and Rare Diseases Advisory Group for discussion. The final version was then co-signed by ministers of each of the four nations.[13]

Rare Diseases Framework Governance



The UK Rare Diseases Framework is led by a steering group (the UK Rare Diseases Framework Board), which meets twice a year to provide high level alignment and co-ordination of rare disease policy across the four nations. It is supported by the UK Rare Disease Forum, a channel for engagement with the rare disease community, which conducts formal meetings and runs an online platform for stakeholder discussion.[14] From an operational perspective, each UK nation then has its own group which leads on action planning and is responsible for tracking progress and new opportunities in annual updates.[14]

Source: England Rare Diseases Action Plan 2022[15]

Phase one: The UK Rare Diseases Framework

Published in 2021, the UK Rare Diseases Framework sought to refresh the approach to rare disease policy and provide the basis for driving improvements over the next five years. It set out a vision for addressing health inequalities, improving the quality and availability of care, and delivering better outcomes for people living with rare diseases.[4]

The Framework identified four key priorities, which had been highlighted as major challenges by the rare disease community:

Priority 1: Helping patients get a final diagnosis faster	Getting the right diagnosis is key to effective management of rare disease, however, it has been consistently highlighted as one of the most significant challenges faced by the rare disease community.
Priority 2: Increasing awareness of rare diseases among healthcare professionals	It is important that healthcare professionals are aware of rare diseases more widely, alert to considering them, and are provided with the education and resources that can help them recognise rare diseases in patients and be aware of potential specialist treatment needs.
Priority 3: Better co-ordination of care	Coordination of care is essential to ensure care is effectively managed, the burden on patients and their carers is minimised, and healthcare professionals are working together to provide the best possible joined up and high-quality care.
Priority 4: Improving access to specialist care, treatments, and drugs	Patients need to have access to expertise in the treatment and care of their rare disease where available, and there are opportunities to develop innovative models of care across the healthcare system so that patients have their care delivered as locally as possible.[4]

These are underpinned by five '*themes*', which were identified as being needed to support future progress on the four priorities: patient voice, national and international collaboration; pioneering research; digital, data and technology; and wider policy alignment. Each priority and theme are explored in further detail in the report.

Overall, the priorities and themes identified in the Framework follow on from the 2013 UK Strategy for Rare Diseases.[16] This includes a focus on faster diagnosis – which both publications recognise as being vital to reducing the risk of mortality and morbidity – as well as coordination of care - setting out the necessity of multidisciplinary teams (MDTs) and joint-working across healthcare professionals.

Phase two: National Rare Diseases Action Plans

This phase of the UK Rare Diseases Framework mandated devolved governments to develop implementation ('action') plans, highlighting how the aims of the framework would be met at a national level. Developed in close collaboration with the rare disease community and published in 2022, the inaugural action plans set out focus areas and actions for taking change forward in each of the four nations.[14,17,18,19] Overall, the plans are notable for a heavy focus on rare genetic and inherited diseases, with less policy focus on rare disease acquired later in life.[17,18,19]

England

England's second Rare Diseases Action Plan[20], published in February 2023, assesses progress against the actions included in the 2022 Action Plan, as well as setting out 13 new specific measurable actions, which have been developed in consultation with the rare disease community. It recognises that "*delivery has taken place against the backdrop of a challenging environment*,"[20] and as such, some actions from 2022 will be carried forward as not all milestones have been met, however, "*significant progress has been made*" overall.[20]

Stakeholder response to the publication of England's 2023 Action Plan was positive, with Genetic Alliance UK applauding the announcement of dedicated research funding into care coordination,[21] and the Association of the British Pharmaceutical Industry (ABPI) welcoming its commitment to review the effectiveness of the UK's early access mechanisms.[22]

Wales

Published in June 2022, the publication of the Wales Action Plan 2022–2026 was also welcomed by rare disease stakeholders, noting the involvement of the patient community in getting mental health and transition to adult care included as key priorities for implementation.[23] Other notable developments in the Welsh Plan include the funding of the UK's first Symptom Without a Name (SWAN) clinic in Cardiff, which will offer genome genetic testing to seriously ill children. The Rare Disease Implementation Group, in conjunction with the Welsh Health Specialised Services Committee (WHSCC), health boards and other partner organisations, will be responsible for the prioritisation, delivery and oversight of the Plan.[24]

Scotland

The first Rare Disease Action Plan for Scotland was published in December 2022. The Plan, comprising 18 actions, outlines the Scottish Government's initiatives for the next 18-24 months, in collaboration with the Rare Diseases Implementation Board, NHS Scotland, and third sector partners. While the Plan is understood to evolve over time and be reflective of the changing rare disease landscape,[17] an update on its progress has not yet been published, and it has received over £1 million in funding support.

Northern Ireland

The Rare Disease Action Plan in Northern Ireland was well received by industry, which heralded it as a "*big step forward*" for rare disease care and welcomed its commitment to review the Managed Entry of New Medicines process.[25] Developed under the leadership of Chief Scientist Professor, Ian Young, it has faced some setbacks in its implementation due to the political stalemate which sees Northern Ireland without an Executive at Stormont.[26] Some actions have faced delays as they require ministerial approval, such as the creation of a new genomics service. Five working groups, involving the NI Rare Diseases Partnership (NIRDP), and backed by the Department of Health, work on the plan's objectives and have been set-up as part of the Northern Ireland Rare Diseases Implementation Group.[26]

The future of rare disease policy

Whilst it is promising to see these Action Plans being published and the inclusion of commitments to monitoring and reviewing their implementation, it is worth noting that progress has fallen behind schedule owing to both political and external factors. For example, in Northern Ireland, the political situation and absence of Government has slowed down activity and across all countries the well-documented pressures faced by health systems risk delaying progress. For this reason, continued focus on and accountability for the delivery of the UK Rare Diseases Framework is needed, particularly as we know this policy document has an expiry date.

With the Rare Diseases Framework, and the priorities contained within it, focusing on the broad drivers of improvements in care, we believe that there is value in showcasing rare disease services that are functioning well and can provide specific examples of best practice to others. The PNH National Service provides an interesting example as a stable and internationally recognised vanguard, which could provide a roadmap for services overseeing the diagnosis, treatment and ongoing care and management of other rare conditions to follow.

Overview of PNH and the PNH National Service

About PNH

PNH is a chronic, rare, acquired blood disorder characterised by the susceptibility of blood cells to attacks from the body's immune system.[27] Its onset can be sudden, and, as a rare disease, patients can find the experience of diagnosis isolating – with lifelong treatment to manage a range of debilitating symptoms often making their lives vastly different to pre-diagnosis.[28]

PNH develops when a patient’s bone marrow produces cells that have mutations in the ‘PIG-A’ gene. This gene is responsible for producing a protein, the ‘GPI-Anchor’, which protects normal blood cells against the body's own immune system. The lack of certain proteins on the blood cell surface means that these PNH blood cells are not protected against one of the body’s normal immune responses to help fight infections (the “complement system”).[29] This lack of protection allows the immune system to destroy PNH blood cells and results in the destruction of red blood cells (“haemolysis”), which is the main cause of the range of symptoms and complications related to PNH.[29]

Haemolysis leads to various symptoms, although how the condition presents itself may differ across patients and some patients may exhibit no symptoms at all. Typical symptoms of PNH include:

- Haemoglobinuria (dark or black urine, as a result of haemolysis)
- Difficulty swallowing
- Abdominal pain
- Breathlessness
- Erectile dysfunction
- Kidney damage
- Anaemia
- Fatigue
- Jaundice
- Blood clots[30]

Diagnosis of PNH typically involves blood tests, with a flow cytometry test to confirm the presence of PNH blood cells.[31] Flow cytometry testing is established as the method of choice for diagnosing PNH and is key for monitoring patients.[32]

The impact of PNH on patients

Estimates of the number of people affected by “haemolytic PNH” range from one to nine in a million,[29] whilst another ten people per million have a small PNH clone but fewer symptoms.[27] It is estimated that there are between 650 to 900 people in England living with the condition,[33] although the true number may be higher.[34] PNH can occur at any age but is most frequently diagnosed between the ages of 30-40 years old.[33]

Treatment for PNH tends to be lifelong and aimed at alleviating symptoms and reducing the risk of complications, rather than curing the condition altogether. Patients living with PNH describe various wellbeing impacts, including feelings of loneliness of living with a rare condition, fatigue, and disruption to employment and social activity.[35]

Existing treatments include:[36]

- Blood transfusions, to alleviate anaemia
- Folic acid, to support the production of blood cells by the bone marrow
- Anticoagulation, to reduce the risk of developing blood clots
- Iron supplements or iron removal, to ensure stable levels of iron in the body
- Complement inhibitors, to protect the PNH cells from destruction

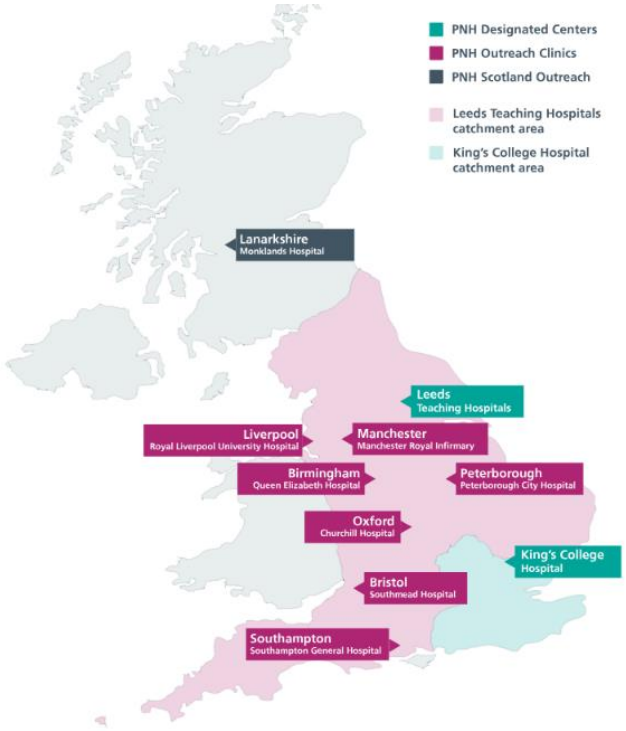
For example, PNH can lead to severe anaemia, often meaning patients need regular blood transfusions for extended periods (if not indefinitely), which are delivered by local hospitals as part of shared care agreements.[37] Fatigue is commonly cited as severely impacting patients' ability to carry out day-to-day activities, often impacting work and social commitments.[30] In PNH, pregnancy is associated with potentially high risk, primarily due to thrombotic complications.[38] This is a particularly pertinent quality of life issue, as patients typically receive a diagnosis of PNH in their thirties and forties i.e., at a potentially important time for family planning.

The UK PNH National Service – an overview

The gold standard UK PNH National Service has accumulated a unique wealth of experience, thanks to the significant volume of patients (for a rare disease) under its care.[39] Funded today by NHS England as a highly specialised service, it was established in 2009 to provide the highest quality management of PNH patients throughout England, with agreements in place to provide care for patients from the Devolved Nations.[40] The Service provides diagnosis, clinical review and ongoing management for patients with the haemolytic form of PNH who are eligible for treatment with anti-complement targeted therapy.[41]

Commenting on the Service in the Rare Voices report, published by the Together for Healthy Bone Marrow Alliance, Dr Morag Griffin, Consultant Haematologist, said "the PNH service consider it a privilege to be able to offer patients a gold standard service for rare disease. The model of care delivery is considered an example of excellent care by other PNH services worldwide and can be used as a template for other rare diseases with similar patient numbers as PNH."[42]

A geographical overview of the National PNH Service



The Service comprises two designated centres – King's College Hospital, London and St James's University Hospital, Leeds, – and a network of eight outreach clinics.

Patients are referred to one of the centres following PNH diagnosis (usually by a local haematology service), depending on location: patients from London and the Home Counties are referred to King's College Hospital and patients from elsewhere are referred to the service at Leeds. Patients referred to the Leeds service are reviewed in the PNH clinic either in Leeds or one of the outreach clinics. The Leeds PNH Centre is also responsible for managing patients from Scotland (in the Lanarkshire clinic), Wales (seen either in Bristol, Manchester, or Leeds), and Northern Ireland (seen in Belfast (remotely) and Leeds).[43]

Source: PNH National Service[39]

Service delivery is based on a model which ensures that the patient journey is the same at each commissioned centre. The service aims to provide treatment and follow-up as close to home as possible, and care is delivered through a hybrid model of face-to-face and virtual appointments,[44] with some treatments delivered by local haematology teams or via home delivery. Specialist PNH clinics are held on a weekly basis at the two centres and Consultants and nurses from the PNH National Service in Leeds travel to each outreach clinic with a frequency of between every six weeks (Birmingham) to six months (Oxford and Southampton), with the dates of their visits published on the PNH National Service website.[44]

Patients are evaluated in clinic and monitored for organ damage and complications relating to disease progression and prescribed appropriate treatments. Weekly multidisciplinary team (MDT) meetings are held at both centres to discuss patient issues, and the centres work closely together to agree patient management plans, with monthly shared MDT meetings. All patients are managed by the Service through a shared care agreement with local haematology units.[40] This ensures that patients receive specialist oversight by the National Service, whilst also having a local point of contact in between appointments who are able to manage some symptomatic treatments and any health problems separate to the PNH.[45] While the Service manages all elements of complement inhibition for

PNH for patients in England, local haematologists prescribe for patients in Scotland, Wales, and Northern Ireland under the direction of the Service.[40]

The service provides a 24 hour, 7 days a week on-call service with patients having direct access to a PNH specialist consultant and/or a haematology consultant (depending on location) for advice relating to the disease or therapy, particularly to ensure rapid and appropriate management of complications.[43] A website has also been developed to ensure that appropriate and up-to-date information is communicated to patients regularly.

The laboratory diagnosis and follow-up of PNH, which requires specific expertise, is made at both the haematological malignancy diagnostic service (HMDS) in Leeds and the haematology malignancy diagnostic centre (HMDC) at King's College, using the same flow cytometric technology that is considered the gold standard for testing.[43]

The PNH National Service is also notable for its involvement in clinical trials. The service website states that it aims to offer all patients with PNH who are eligible for a clinical trial the option to consider participating in one, which is discussed with the specialty team at clinic appointments.[46] According to data from its most recent annual report, the PNH National Service saw 1,025 patients in the year to April 2023.[47]

PNH and the Rare Diseases Framework Priority Areas

This section considers how the PNH National Service provides a case study in best practice for rare diseases in how to work towards achieving the goals set out in the Rare Diseases Framework. It is based on the insights that we have gathered from engagement with staff from within the PNH National Service through structured interviews. All quotes within this section have been pulled directly from these structured interviews.

Priority 1: helping patients get a final diagnosis faster

The Rare Diseases Framework highlights the well-recognised 'diagnostic odyssey' that is experienced by many patients who have a rare disease, with the route to diagnosis often involving numerous referrals, inconclusive tests, and incorrect diagnoses before a conclusive final diagnosis is reached.

Internationally, low recorded incidence rates and our research points to PNH being significantly underdiagnosed and therefore a PNH patient's journey to receiving a diagnosis is often not that different from other rare diseases. Data underlines a higher prevalence of PNH in the UK versus other countries[48,49] which could suggest better diagnosis rates. The National PNH Service recommends the ICCS guidelines in relation to testing for a diagnosis of PNH.[50]

Nonetheless, the UK has the potential to do even better. Clinical experts involved in PNH care acknowledged that patients could experience barriers to diagnosis, particularly as a consequence of how symptoms are assessed when

these patients first present to the NHS (e.g. general practice) and generally low awareness of PNH across clinical specialties beyond haematology.

PNH symptoms can often mean that patients are first referred to specialties other than haematology, for example, presentation with haemoglobinuria means referral to urology is particularly common. Other specialties that could commonly receive PNH patient referrals include gastroenterology, due to the associated abdominal pain, and stroke physicians, where patients present with blood clots. Members of the PNH Service agreed that patients are typically diagnosed fastest when they receive a referral to a haematologist, where it is much more likely that the flow cytometry test used to diagnose PNH will be requested.

> "*Some patients are diagnosed very quickly…some people can take up to 10 years…one good thing about PNH compared to any other rare diseases is once you suspect, the diagnostic testing is extremely sensitive and specific so it's just getting to that stage of saying 'let me do a PNH test'.*"
>
> **PNH Service Team Member**

Whilst flow cytometry is easily accessible and able to provide a quick diagnosis for PNH, it must be ordered as part of a diagnostic investigation. Clinicians underlined that one of the main barriers to earlier diagnosis is that PNH may not be conceived of as a potential diagnosis when a patient is first referred, leading to delays in accessing the right diagnostic interventions. In relation to testing for PNH, it was also noted that larger hospitals are better set up to include PNH in a large order set for blood testing, making it more likely that they will receive a faster diagnosis.

The Rare Diseases Framework underlines that without the right diagnosis, it is difficult for patients to access the best treatment for their condition. Those working in the PNH Service highlighted that, for PNH patients, delays in diagnosis can lead to negative impacts, including progressing severity of symptoms, increased risk of thrombosis, alongside the impact of going through unnecessary investigations. It was noted that PNH testing is a standard element of investigations in some specialties, for example younger patients presenting with blood clots will often receive a PNH test when they are seen by a stroke physician, but this is an exception to the general absence of PNH testing from investigations under other specialties.

It was noted that there has been steady progress to speed up diagnosis for PNH patients and that, once a patient is referred to haematology, a diagnosis can be reached quickly, followed by a rapid referral into the PNH National Service. Members of the service highlighted that faster diagnosis had been achieved through a concerted effort to raise awareness of PNH across the haematological community, through engagement with the deaneries of haematology units to ensure that the curriculum includes PNH.

Priority 2: increasing awareness of rare diseases among healthcare professionals

The Rare Diseases Framework recognises that the nature of rare disease makes it difficult for healthcare professionals to be familiar with every specific rare condition that might be experienced by their patients. With over 7,000 rare diseases, it is not possible to provide specific education on each condition, and the Rare Diseases Framework underlines that this necessitates, instead, that healthcare professionals have a general awareness of rare disease and are prompted to consider the possibility of a rare disease when treating and referring a patient.

The PNH National Service plays an important role in supporting awareness of PNH as a condition. This is particularly true in relation to haematology, with members of the PNH service regularly engaging in educational opportunities with regional haematology teams and speaking at national and international conferences.

Clinical experts involved in the PNH Service play a crucial role in raising the profile of PNH with other specialties. Recent educational engagement has included seminars for clinicians specialising in renal care, hepatologists, urologists, gastroenterologists, neurologists, and general practitioners. The PNH Service leaders highlighted the importance of pragmatism in relation to raising general awareness of PNH in other specialties, noting that a rare disease by its nature is difficult to keep front of mind for those who do not encounter the condition as regularly.

For this reason, it was noted that the central focus of awareness raising efforts has been engagement with haematologists, to support the rapid diagnosis of patients once they have been referred here. Clinicians noted that there were often opportunities to talk about PNH as part of wider education initiatives in haematology, recognising that the rarity of PNH demanded that it is raised in the context of wider areas and issues relevant to haematology.

It was also recognised that education to support PNH not only includes awareness of PNH as a condition, but also awareness of the PNH Service itself, so that local haematologists can refer patients as soon as possible. Awareness of the Service is perceived to be high, with there being a quick process for patients coming into the service following diagnosis.

In relation to clinical awareness of the impact of PNH, for example on quality of life following diagnosis, it was observed that a key benefit of the PNH Service is the support that is provided across a patient's health and wellbeing needs. This ensures that patients have an advocate around their condition, via the national service, to support any engagement they might require with other clinical specialties, thus reducing a reliance on awareness of PNH across other specialties to effectively understand and manage the impact of PNH on patients.

Priority 3: better co-ordination of care

The Rare Diseases Framework notes that the management of rare conditions can be complex and often requires involvement from multiple specialists. This means it is very important that care is coordinated effectively, in a joined-up way around the patient, across the various specialties and services that are relevant to patient care.

The PNH National Service is an exemplar in the way in which care is coordinated, with the service providing an anchor point for all elements of PNH care, including co-ordination with other specialties as needed and wrap around support for patients.

Following a diagnosis, a new PNH patient will be referred to the service and will receive an hour – 1.5 hour consultation, to discuss the condition and start to develop a treatment plan (for those patients who require treatment, as opposed to ongoing monitoring). This consultation is led by a consultant within the PNH Service and will also involve a specialist nurse.

"The ethos of what we do is to provide a service…we're not limited to how much time we spend with people. It's important that [patients] get access to someone who knows about their condition and knows what they're going through, and what to do to help them."

PNH Service Team Member

Members of the PNH National Service underlined the crucial role of the specialist nurse in coordinating care around a specific patient, as well as their role in coordinating the services, for example the management and administration of home care teams who will support patients to receive outpatient treatment once they have a treatment plan in place.

The service within King's College Hospital has access to an in-house psychological specialist who is available to support patients. In addition, wider issues that might be impacted by the condition, such as employment and housing, are areas where patients can receive support from a dedicated social worker. Leads within the PNH Service explained that this allows care to be coordinated effectively and for wrap around support to be led by the Service.

The value of this standard of care is evidenced in reported patient experience from those who use the PNH service, with a higher proportion of people with PNH (77%) feeling supported by services (healthcare and/ or charity/patient groups) than people living with other rare conditions affecting the bone marrow (63%).[42]

A specific area of care coordination with other specialties that was highlighted was coordination with obstetrics and gynecology to support PNH patients with maternity needs. The progress made through the availability of the Service was particularly noted in this area, with pregnancy historically viewed as an absolute contraindication for PNH, but through the advent of treatment and effective coordination of care this has transitioned to such an extent that 20 babies have been born under the supervision of the King's team.

"We work very closely with our obstetricians, they know exactly what we are aiming for, what we are looking for. Our obstetricians are very well aware of high-risk pregnancies...More often than not, with care, monitoring, treatment and working very closely with specialties with clear levels of communication it's possible to take people through their pregnancies."

PNH Service Team Member

Care coordination, including close working between the PNH National Service and local haematologists helps to reduce the burden on patients in relation to travelling for consultations and hospital visits, with most patients being seen within the service every 3-6 months. In the intervening period, the PNH National Service team work closely to direct care with local teams. This includes the provision of a 24 hour emergency service, that patients can use to access clinical and other support. For example, the on-call service might be contacted to support a PNH patient presenting to emergency services following a fall, with the PNH clinician able to provide immediate input and advice on how care should be adjusted in response to PNH. It was highlighted that the involvement of the service extends to support internationally, with the service being connected to PNH specialists around the world that can be engaged to deliver care to PNH patients should they need it during travels outside of the UK.

Members of the service emphasised that the whole ethos of the PNH National Service was to deliver excellent, joined up care around the specific PNH patient and to ensure as far as possible that the condition is well managed, so that patients can lead life to the fullest. Care co-ordination, including the significant accessibility of specialist clinical and non-clinical support around the clock, is at the heart of meeting the ambitions of the service.

Priority 4: improving access to specialist care, treatments, and drugs

The Rare Diseases Framework recognises the importance of access to treatment for rare disease and developing a UK environment that enables access to new treatments and innovations in care.

Members of the PNH National Service emphasised that patients have good access to specialist care and treatment – which is supported by the engagement of the service in clinical trials. Clinicians highlighted that it is a priority to recruit patients on to trials, for example, the Leeds service is likely to have approximately 50 patients participating in clinical trials at any given time.

It was recognised that shared decision-making was an important part of how patients are supported to make informed decisions about their care and that patient support groups play an invaluable role in sharing and developing information to support this. It was noted that this also means the PNH patient community is often very well-informed of developments in new treatments and engages with the Service on this.

"Compared to other medical problems…I think once a patient is registered…I've not heard any PNH patient complain that it's been hard for them to access medical advice or care for PNH. The PNH patient support organisation does a huge amount to educate patients… we always signpost people to the groups."

PNH Service Team Member

Members of the Service also highlighted the value of clinical trials to the wider NHS, enabling patients to access new and innovative medicines whilst reducing direct costs to the health system. This was underlined as an important area in which the PNH Service delivered value not just to the PNH community but to the health system more widely.

PNH and the Rare Diseases Framework Underpinning Themes

Patient Voice

Professionals working in the PNH Service emphasised the importance of patients in its development, both when it was first established and on an ongoing basis to ensure that it is meeting patient needs. Members of the team highlighted the relationships between the Service and PNH support groups, providing direct opportunities to hear from patients.

Additionally, those working in the Service noted that the way in which the service is run, with such a high degree of involvement in coordinating patient care, often means that consultants have an established relationship with patients and are well-informed about what is happening in their life and their specific needs. The relatively small team also enables a consistency in care that was seen as a beneficial element to supporting and empowering patients.

It was noted that the development of patient support networks was contiguous with the establishment of the National Service and these two important aspects of delivering world class support to patients in the UK went hand in hand. The value of these relationships in relation to patient empowerment is evidenced by recent research on rare bone marrow conditions, which found that 50% of PNH respondents know where to access the information needed to help manage the condition, compared to 39% of all other condition respondents.[42]

National and International Collaboration

Numerous examples of national and international collaboration were highlighted by members of the PNH service, including the role of clinicians in international conferences on PNH and in the haematology space more broadly to support awareness of the condition.

Some specific areas of international collaboration include the International PNH Interest Group (IPIG), that fosters connection around the world and provides a forum for clinical expertise to be shared. Clinicians highlighted the advent of the IPIG's first international conference in 2023, and the opportunity it provided for those working in PNH to come together. In addition, members of the service will attend other international haematology conferences, such

as the American Society of Hematology (ASH) conference and European Haematology Association (EHA) conference, where there will be dedicated time allocated to focus on PNH for world experts on PNH to come together.

"Because it's a rare disease, there are very small numbers of clinicians around the world who treat it and we all know each other... Almost everything is done collaboratively, I don't think there's anything we're doing that doesn't involve international collaboration."

PNH Service Team Member

A further area of international collaboration is the establishment of an international registry for PNH, which has been created by the IPIG, to gather epidemiological data on PNH and provide opportunities to use it as a research mining tool. The registry is led from Leeds, with consenting patients joining to provide information about their condition that can support learning.

Pioneering Research

The PNH National Service is very active in pioneering research through trials for new treatments, as well as supporting better understanding of PNH. Clinicians working within the service highlighted the importance of supporting patients to access clinical trials and the role that the service has played in supporting innovations in therapies for PNH, with patients benefiting from innovations that have arisen since the initial establishment of the service in 2009.

"[The service has] a very active interest in clinical trials. The starting point with any patient is to see whether they can be recruited to a trial, because there's a lot of evidence that patients do better on clinical trials, so at least giving them the option is something we do for everybody."

PNH Service Team Member

In relation to pioneering research into understanding of the condition, it was highlighted that research is being taken forward focused on understanding the underlying cause of PNH, which is not yet known, and that this is a key area of interest for the service. Clinicians referenced the role that research led by the service can play in understanding the science behind patient responses to different types of treatments, to support developments in approaches to care. The PNH National Service also co-ordinates a PNH tissue bank, which facilitates research in a number of areas. The response to COVID-19 was highlighted as an area in which the tissue bank had been important, enabling research into vaccine responses to support the pandemic response in relation to PNH.

"[The service] being involved in research is really important. A specialist in the States might have 30-40 patients, we've got 1000 across the UK. We're in a unique situation where we have a national service, and we can provide answers to questions that a specialist in another country might not be able to"

PNH Service Team Member

Digital, data and technology

The Rare Diseases Framework makes clear that digital, data and technology are a critical element of improving care for patients across the NHS, including steps to adopt digital innovations effectively and ensure the interoperability of health systems' data infrastructure.

Members of the Service highlighted the impact of the pandemic on service delivery and the transition that had been made to virtual consultations with patients as a result. This was generally recognised to be a benefit to patients and a development that offers flexibility to support a better patient experience.

It was noted that, in relation to data, there is a wealth of data about patient experience and patient outcomes that will be collated through the PNH registry, which should be leveraged in the future to support clinical innovations and optimisation of patient care, both generally and on a personalised basis. This includes the potential to use technology, such as apps, to capture live data from patients through their day to day lives. It was observed that these areas were of growing interest to those who are involved in PNH care, however adoption of such technology was not yet underway.

Additionally, members of the Service highlighted the digital and data infrastructure within the NHS as a challenge. Whilst this is not specific to PNH, it was noted that the nature of care co-ordination through the Service, and the integral role that the National Service plays in directing care locally to the patient makes interoperability of IT systems highly important. It was underlined that this is a current challenge, with clinicians in local hospitals unable to access test results and other information from the national service and vice versa.

Wider Policy Alignment

In relation to wider policy, the Rare Diseases Framework recognises that there are areas beyond health policy that might need to be considered to improve outcomes for people living with rare disease, such as education, housing, and employment.

The comprehensiveness of the PNH Service often means that patients can have wider concerns that may be impacted by their condition addressed through the service, for example, through access to the social worker that is part of the national team. It was emphasised that, through the ambition of supporting patients to live an 'ordinary' life following diagnosis, the Service often would support patients to make others aware about their condition, for example letters to employers to support management in the workplace (with some PNH patients receiving treatment in their place of work from a home care team as a matter of course).

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