PBC uncovered

Patients and clinicians set a new vision for primary biliary cholangitis in Scotland

This report was initiated and funded by Ipsen UK and was produced in collaboration with the PBC Foundation

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Contents

Foreword

By Robert Mitchell-Thain, Chief Executive, PBC Foundation

I welcome the publication of this important report on Primary Biliary Cholangitis (PBC) in Scotland.

This report and its recommendations, based on interviews with patients, patient advocates and clinicians, reflect the unique challenges faced by individuals living with PBC, as well as their families, caregivers, and the healthcare professionals dedicated to supporting them.

For many, a diagnosis of this autoimmune liver disease can mark the beginning of a life-changing journey. The burden can extend far beyond the most common physical symptoms of fatigue, brain fog and indescribable itch, to emotional and psychological harm, unjustified feelings of guilt and stigma, and practical challenges to daily living.

For some, the medicines that they will take daily for the rest of their lives are enough to prevent their livers deteriorating. For others, at the other end of the spectrum, the only treatment option may be a liver transplant.

The authors of this report have sought to reflect how different this condition can be for different people. They have also captured the lack of uniformity and consistency in the identification, diagnosis and treatment resources and pathways in different parts of Scotland.

As the Chief Executive of the PBC Foundation, a Scotland-based charity supporting more than 20,000 patients across the globe, I am proud to see our work reflected in this report.

At the Foundation, we provide vital resources, including our smartphone app which offers accessible information about PBC and allows patients to participate in surveys that inform our policy work. Access to this app has not only improved patient self-management and mental wellbeing but has also equipped us with invaluable data to advocate for evidence-based and meaningful changes in patient care.

We are developing a clinical global impression rating scale to measure symptom severity, treatment response, and the efficacy of treatments for PBC. This initiative will pave the way for more research into PBC and treatments aimed at reducing the burden of symptoms.

Our ambition remains that 90% of PBC patients receive at least 90% of the care recommended by PBC guidelines. Until we have both the best diagnostic system and a national consensus pathway informed by patients – and uniform access for every patient to clinical experts in PBC – then our ambition may be hard in some places to reach.

The findings and recommendations in this report align with our mission, reflecting the voices of the PBC community. We welcome the support of Ipsen in commissioning this report, and the interest of Scottish policymakers in working with us to take its recommendations forward.

1. Context

Primary biliary cholangitis (PBC) is a rare autoimmune liver disease affecting predominantly women.

At a meeting in the Scottish Parliament to review the first draft of this report, Dr Stephen Barclay, a Consultant Gastroenterologist at NHS Greater Glasgow & Clyde, said nine in 10 PBC cases are seen in women, who are typically diagnosed in middle age. He noted that while considered a rare condition, in common with many other autoimmune diseases, the incidence is increasing.

Some 60% of people diagnosed with PBC have no symptoms. Others can experience intolerable itch, fatigue, 'brain fog' and gastrointestinal symptoms. Often, its onset coincides with menopause. It is diagnosed through a blood-based assessment, while the extent of the scarring to a person's liver is primarily identified by FibroScan® ultrasound scanning. If not controlled, the damage to the liver can be progressive. Although a rare disease, PBC accounts for approximately one-tenth of liver transplant activity in the U.K.[1]

Ipsen and Ettrickburn, a Scottish policy and communications consultancy, undertook a series of interviews with patients and clinicians to allow them to share their experience of the condition with a view to examining how Scotland can ensure the approximately 1,900 people affected can be diagnosed and access treatment swiftly and enjoy the best support, information and care wherever they live.

This work was commissioned by Ipsen Ltd, a pharmaceutical company with a focus on rare liver diseases, involving a series of interviews with patients and clinicians. A draft report was then discussed by a wider group at a meeting in the Scottish Parliament on 30 October 2024.

We would like to thank all those who gave their time to be interviewed and then to review a draft version of this report. We would like, in particular, to commend the work of the Edinburgh-based global charity, the PBC Foundation, without whose support we would not have been able to speak to such a diverse cross section of people affected by PBC.

We are delighted to publish this final report in partnership with the PBC Foundation.

2. Executive summary

We undertook interviews with six clinicians and five patients. Their input has been collated in Section 4 The Narrative. We found:

- There is a marked difference in patients' experience of how they receive their diagnosis of PBC and the support and information available to them then and thereafter.
- A diagnosis of PBC can be made from the results of a liver function test using a blood sample. However, opportunities to complete a diagnosis are being missed. Around one in five of these tests, which are undertaken for a range of conditions, will be found to be abnormal. However, less than half of these will lead to further investigation.
- The level of knowledge and understanding of PBC among GPs and non-specialist secondary care clinicians varies, leading to inconsistent diagnostic timelines, and delays in referral and treatment.
- Treatment of PBC is rooted in the need to prevent cirrhosis (severe scarring) of the liver and the associated deterioration in its function. For many patients, this can be achieved successfully with first-line treatment – daily tablets taken on a lifelong basis. For some, the first line treatment is not well tolerated or ineffective. A small number of these patients may go on to need liver transplant.
- Although resources have been shared to guide healthcare professionals in their management of PBC patients, a UK-wide audit suggests best practice is not being met in many cases: over one third of those on the first line therapy are not receiving a high enough dose of the medicine, and nearly half of those at higher risk are not on a second-line therapy.
- Information sources at diagnosis are often poor. Patients reported trying to find information themselves, and not having a clear understanding of their likely prognosis, causing uncertainty and anxiety.
- Clinicians devote a considerable amount of their time to finding effective second-line treatments, with patients often asking them to prioritise finding an effective treatment for their itch.
- Models of care are evolving. Ongoing care is entirely delivered in secondary care, in some places by physicians and in others by nurses or pharmacists, face to face and at phone clinics.
- The symptoms experienced by many PBC patients can have a significant impact on their quality of life and their ability to carry out routine activities of daily living.
- The principles of Realistic Medicine, that seek to encourage patients to be partners in decision-making about management of their illness, are not being met in the ongoing care of some patients with PBC.[2]
- Some patients reported challenges getting GP practices to collect blood samples to monitor the condition, and when they asked the practice for the results of their tests. Others experience long delays getting test results.
- There is no single source of information for newly diagnosed patients. Charities are regarded as the most reliable source of online information. Scotland's *NHS Inform* website[3] only lists PBC as a condition and provides no information for patients.

3. Recommendations

- A national consensus pathway – developed alongside patients – should be rolled out for people with PBC, enabling consistent integrated (primary and secondary services) multi-disciplinary diagnosis and care of people with PBC. Such a pathway should give identification and treatment of symptoms equal priority to prescribing interventions that seek to arrest damage to people's livers. The national Centre for Sustainable Delivery Gastroenterology Specialty Delivery Group should be considered as an enabler for this pathway.

- Consideration should be given to establishing regional PBC expert teams to provide clinic services, both locally at the centres where they are based and in outreach to smaller hospitals to address disparities between larger and smaller hospitals. This model should be underpinned by a national PBC multi-disciplinary team forum that brings together professionals from across different NHS boards to support consensus-based treatment decisions.

- All healthcare professionals should take into consideration the emotional impact of a PBC diagnosis when first informing a patient that they have PBC, ensuring access to appropriate information about the condition. As with all chronic conditions, some patients may benefit from support from mental health services.

- NHS Inform and Public Health Scotland should work with specialist clinicians, the PBC Foundation and British Liver Trust to ensure appropriate NHS-endorsed information is available to every patient at the point of diagnosis.

- All clinical leaders responsible for overseeing a clinician team providing secondary care liver services should ensure that every member has a working knowledge of PBC, its causes and nomenclature, and what is expected of them in delivering best patient care, not least that there should be an opportunity to talk about itch and other symptoms at every consultation.

- NHS Education for Scotland should be invited to develop a Practice Based Small Group Learning (PBSGL) module on rare liver diseases, including PBC, to support continuing professional development health professionals across the primary care workforce.

- People with PBC should be encouraged to be partners in their own care, involved in the co-design of their individualised care management plans that include regular communication of their blood/scan results, potentially through an existing or new patient and clinician smartphone app, or on the forthcoming National Digital Platform for Scotland.

- NHS National Services Scotland should support Scotland's NHS boards' laboratory network to prioritise putting in place the necessary systems for the universal introduction of the Intelligent Liver Function Test.

4. Narrative

Route to diagnosis

As a rare disease, PBC is unlikely to be tested for per se. Instead, particularly in patients with few or no symptoms, it is often only when they have a liver function test as part of routine monitoring for other conditions – and if their clinician seeks further tests where abnormalities are present – that they are diagnosed:

> **"There are a lot of patients that are picked up who are relatively asymptomatic, have liver function tests checked for another indication, often through a kind of health check for diabetes or hypertension or cholesterol, and will be noted to have abnormalities which will then trigger a liver screen."**
>
> **Clinician 3**

> **"Historically, people would just have abnormalities, and it would have been ignored unless they got bad. Now we expect that, if a patient is being investigated, their GP would order a blood liver screen including antibodies. This allows us to triage and prioritise patients when we think there is an autoimmune diagnosis or viral hepatitis, for instance."**
>
> **Clinician 2**

> **"I had an accident at work in the hospital where I work – completely unrelated and they did a blood test, found some abnormalities and sent a letter to my GP. I had another blood test around two months later which showed some abnormalities and was then contacted by my GP to say something was seriously wrong and they were referring me to hospital. Around four months later I went to hospital and received my diagnosis and a FibroScan straightaway in a one-stop-shop. In hindsight, I was actually probably quite unwell and was simply putting it down to being busy or the menopause."**
>
> **Patient 4**

At a Scottish Parliament meeting to discuss a draft of this report, Dr Ruairi Lynch, a Consultant Hepatologist and Gastroenterologist at NHS Tayside, said that more than 20% of routinely checked liver function tests are abnormal but fewer than 50% of these are then investigated further.

General practice in Tayside and Fife has access to Intelligent Liver Function Testing (iLFT) which reflexively refers laboratory samples for further analysis based on initial results. This combines an automatic second 'cascade' of further tests with patient BMI and alcohol consumption, into an algorithm. A real time report is then generated identifying the most likely diagnosis and recommending next steps in management. The introduction of the test methodology has led to a 43% increase[4] in the identification and diagnosis of liver diseases in the region. There is more information on the iLFT in the appendix.

Being newly diagnosed

For patients with significant symptoms, getting a diagnosis can take months or years and, while some reported it to be a relief that there was a condition with a name that was the root cause of their symptoms, getting the information they wanted about the condition was not straight forward:

> **"It took maybe about three years to be actually diagnosed. So, eventually they did the test and obviously it came back positive and I got a letter. I wasn't actually told in person. Partly I was relieved. But then there were questions – what was going to happen? How long did I have? What did it mean for me, for my children who were too young to understand?"**
>
> **Patient 3**

"I was found to have abnormal bloods. I was told not to drink for six months and then the bloods were repeated. They were worse. That got the ball rolling with more investigations. I had scans and then a liver biopsy. Eventually I went to the hospital and the doctor said, "You've got PBC," and handed me a leaflet. Of course, you're too polite to say anything so I took the leaflet, and he said, "You'll get some tablets."

Patient 2

"It was just after the birth of my daughter. I had joint pains and was very tired – but of course I was a new mum. I was referred to rheumatology and given ibuprofen but quite quickly after that I developed an itch which was quite severe. I had an excellent GP who realised there was more going on so ordered blood tests only to discover my liver biochemistry was off. Then I was sent for a biopsy. I think my diagnosis took about six to eight months which, in the scheme of things, is quite short compared with a lot of patients who go on for years with varying symptoms that they can't get to the bottom of."

Patient 5

While the NHS Inform website run by NHS 24 does not have information for patients on PBC, the clinicians we spoke to often referred patients to the PBC Foundation and the British Liver Trust for **support information**. However, patients can wait sometime between receiving their diagnosis and having an appointment with a specialist – time that many respondents said they filled by doing their own research:

"I got my diagnosis over the phone. I phoned up for the results. It was slightly scary and intimidating to be told you've got an autoimmune condition that you've never heard of. So, I instantly turned to Doctor Google."

Patient 1

"I wasn't actually told in person – I got a letter. So, I did the human thing and started Googling and was thinking I was dying right away because nobody sat down and actually explained anything at that point."

Patient 3

"The information I got from the NHS was very poor. It was one leaflet, but it really didn't tell me enough. I didn't know what was going happen to me, whether it was terminal. And you're just too polite to keep asking questions, you accept what people say."

Patient 2l

"It would be good to have patient facing materials that we could give people to take away with them. We have a selection of little pamphlets about liver conditions, but the correct things are not always to hand and some of the information is quite out of date."

Clinician 6

"It's difficult to have tailored information for every patient with differing degrees of disease where a large proportion will never run towards transplant."

Clinician 4

Treating PBC and its symptoms

The clinicians that we spoke to started patients on ursodeoxycholic acid (UDCA) or 'urso', as first-line treatment immediately on diagnosis of PBC to reduce the risk of the condition worsening. A series of investigations are often undertaken, particularly a FibroScan® which is a form of ultrasound that assesses the degree of fibrosis (scarring) and cirrhosis (long term scarring) of the liver. Where there is cirrhosis, this may be followed up with ongoing scans, while blood monitoring will continue to track the passage of the condition for all patients. Some patients are maintained effectively on ursodeoxycholic acid:

"I've been on urso since 2008 when I was diagnosed. I haven't really had a lot of problems; my blood seems fairly normal. For me, PBC is something that is in the background. I don't have lots of symptoms or problems, so I put it into the back of my mind."

Patient 2

Several clinicians reported that all their **patients not responding** to UDCA would be discussed at a local or even national multidisciplinary team meeting and considered for second-line treatment or a clinical trial. We did not establish whether this is universal across Scotland. Guidelines suggest escalation to a second line treatment if the response after one year on first line treatment has been unsatisfactory.[5]

There are currently on and off licence second line treatment options availabe for patients who have an inadequate response to, or are unable to tolerate, UDCA.

> **"Many people live very normal lives on ursodeoxycholic acid and, if needed, quite well on second line treatments. They live normal lives and die with, not from, their PBC. There is this percentage of people, like me, who are non-responders. It has left me in limbo a wee bit, not being able to take the second-line medication. There's nothing else there at the moment for us which is quite hard."**
>
> **Patient 3**

For clinicians and their patients, treatment decisions are driven as much by **the need to reduce debilitating symptoms** of PBC – particularly itch without a rash – as to arrest the deterioration of the liver. The severity of itch and the severity of the disease (as measured by both liver function test results and scans) may not correlate, meaning that medicines to address itch are prescribed alongside both first- and second-line treatments for PBC.

> **"People can have horrible itch without a particularly nasty blood test. So, you have to focus on symptoms because quality of life is hugely important and if you're failing to treat it then that completely undermines your patient's faith in you."**
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> **Clinician 2**

> **"In regard to itch, you've got bile salts sequestrants, topical therapies, and I would consider rifampicin as my next best go to. I think in appropriate patients it's kind of life changing for patients with itch, in those it works for. Unfortunately, we cannot always treat itch adequately. And then there's optimum management of dry eyes as a symptom, and then make sure they're up to date with their bone screening as well."**
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> **Clinician 4**

> **"I'm now on naltrexone which does the trick, but I really shouldn't be on that for a great length of time and it's been for years now and it's the only thing that stops it."**
>
> **Patient 3**

> **"The itch was relentless. It was like bugs crawling underneath my skin. It felt like fire sometimes it was so hot. My skin would always be broken and bruised. I needed to change the bed sheet every morning because I'd been bleeding overnight, not sleeping. And the world is a very lonely place during the night when you get up in the morning and you're the only person up and cleaning up, trying not to make too much noise in the house because you've got a child."**
>
> **Patient 5**

One clinician suggested that conversations during clinic visits may sometimes be too focused on test results rather than symptoms, while one patient admitted they'd never asked for help with their itch:

> **"I think probably in the past, if the bloods were fine, there wasn't as much focus on asking patients about symptoms. But actually, when you take the time to ask – and people have said to me, "nobody has asked about that before". I have patients reporting symptoms that don't appear to have been discussed, or certainly documented, previously."**
>
> **Clinician 5**

"I've tried every antihistamine on the market for my itch. I'm actually itching as I'm talking to you. The itch is quite bad. I've always bought my own antihistamines and tried as best I can with different creams and lotions. But during the night I am clawing at myself. I just can't stop it. I don't want to go to my doctor. They are so busy, you can't get an appointment and, because my PBC is under control, I don't really want to take up their time."

Patient 1

Another debilitating symptom of PBC is **fatigue**. Although patients lived with both fatigue and 'mind fog', nobody said they felt confident talking about it:

"Today [the registrar] was on about fatigue saying you need to do exercise, which I do all the time, I'm on the go all the time, I very rarely stop. But I tried to explain to him that fatigue and tiredness are two completely different things."

Patient 3

"Fatigue is difficult to describe because you don't know what normal is. I've got two young kids – you're running about, you're a busy mum. Where is the baseline for fatigue? So, when people say, "what are your symptoms?" I don't even mention fatigue. I don't know where I am on the scale of that."

Patient 1

"I don't want to say to my boss, "I feel really knackered, can I sleep in this morning?" or "can I not do that trip?" That's the biggest thing for me. I'm not as sharp as I used to be – a bit foggy minded, and it worries me. I'll be in a meeting with lots of people and they're all asking me questions and I begin to lose track of things."

Patient 4

Mo's Story

Mo Christie told her story of living with PBC. She was diagnosed in 2007 at the age of 36, after feeling fatigued and, later, experiencing itch.

She said she started on UDCA but was a non-responder and saw little improvement. She said her itch became unbearable after a few years, leading to scarring, infections and an inability to sleep. She was referred to Edinburgh Transplant Unit. She was given plasmapheresis therapy that helped reduce her itch, but she explained this was unsustainable long-term due to the huge travel commitment and the time each treatment took.

Mo said she was first assessed for transplant in 2012 and, after exhausting all other treatment options, was reassessed in June 2013 after her quality of life deteriorated further. She waited two weeks before receiving her part-liver transplant. She said her itch disappeared immediately. However, after losing blood supply to her new liver, she was relisted for another transplant. Just 36 hours later she received a whole liver transplant. She said she struggled both physically and mentally and recovery was difficult. However, 11 years later, although Mo continues to manage other PBC symptoms, her itch has not returned which has massively improved her quality of life. Although transplant is effective treatment when it is successful, she said it is by no means an easy option.

Mo said it was only when she was put in touch with the PBC Foundation that she got the information she needed about the condition and started to feel less alone, and that the support of the PBC Foundation during her journey has been very important to her wellbeing. She joined the team full-time over two years ago and now works in patient advocacy.

Transplant

The first goal of treatment is to prevent the liver becoming so damaged that a liver transplant needs to be considered. Clinicians expressed concern that there is an unknown number of patients who remain undiagnosed as their PBC is progressing:

> **"I've had patients that we've picked up who we've simply not known about for years and years. I had a patient last year who I referred for transplant the first day I met them."**
>
> **Clinician 2**

Liver transplant is a major operation with associated risks and potential complications. However, for patients who progress to late-stage PBC, it is their only available option. Transplant may be considered at an earlier stage in the progression of the condition to eradicate a patient's itch.

Some 10% of liver transplants in the UK are for people with PBC[6].

Another patient, who suffers "unbearable" itch as well as chronic gastrointestinal issues due to bile reflux – preventing her from enjoying food – talked of her bitter disappointment at being turned down for a transplant.

> **"You're sitting there in a room with a group of doctors and me and my husband. I've been in hospital all week I've been through all the tests, and you're told basically, "not today, not on this occasion because you're not ill enough". That week there was a woman brought onto the ward. She hadn't known that she had PBC and collapsed at home and was given a transplant. She was up walking, showering and eating. She was amazing. I was happy for her, but you can't help feeling I wish that was me... Nobody wants to go through that, but I just feel I've had enough now and just wish that that was me and that I had a chance of just feeling normal, feeling well."**
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> **Patient 3**

Misunderstanding and stigma

PBC is an autoimmune condition and not brought on by external factors such as alcohol and drug use. In the past, due to the significant damage to the liver (cirrhosis) it caused, the disease was named Primary Biliary Cirrhosis. However, in 2015, this was changed to Primary Biliary Cholangitis to classify the disease more accurately – with effective management the minority of patients develop cirrhosis – and seek to end any stigma arising from the term cirrhosis. For the patients and clinicians who took part in this research, the change was welcomed but not universally recognised – and the questions about why they had developed the condition remain unanswered:

> **"Most doctors know PBC's a liver disease, a lot of them still think it's related to cirrhosis. They struggle with patients who have positive antibodies but not much else, so some don't do further tests. Some diagnose fatty liver disease but don't realise that having fatty liver doesn't stop you having PBC as well. They struggle because PBC is much less common than other conditions."**
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> **Clinician 1**

> **"I think there's definitely more awareness. The name change takes away some of the liver judgement which is a real thing. At first I was too ashamed to tell anyone that I had a liver condition because they would automatically judge that was because of alcohol – that I did it to myself."**
>
> **Patient 4**

> **"I've kept my PBC quite hidden. I understand all about stigma from my professional work and how wrong it is. But the minute they mentioned liver, I was taken aback. I'm not a big drinker but you think "has this been self-inflicted? Have I brought on this autoimmune condition somehow?" Then I am also thinking: my dad died of pancreatic cancer 30 years ago when I was 14. Could there be some sort of genetic connection?"**
>
> **Patient 1**

"I have a daughter. I have a son too and I know men can get it but it's not as common. So, I worry about my daughter getting PBC. I know there's no sign of it in my family, but I also know that it's commonly misdiagnosed or goes undiagnosed."

Patient 3

"It was really hard. The GP said there was something really wrong. I went through a really dark period because I was told to stop my hormone replacement therapy, to stop drinking any alcohol, which I didn't think was a big thing but actually, at the time, was a big change for me. And then when I got the diagnosis, the consultant was great, he answered all my questions. But it was still quite difficult after the diagnosis. It was quite dark."

Patient 4

Patient as a partner

Central to the ongoing care of patients with PBC are periodic **blood tests**. Some clinics arrange for a patient to attend their GP surgery, community hospital or regional phlebotomy hub a couple of weeks in advance so the results can be discussed at their appointment. More than one patient said they had blood taken during the clinic visit and the results were then discussed at their next appointment. Others said they were asked to make their own appointment with their GP practice to get bloods taken.

"My previous GP was brilliant. I would get my bloods done once a month and they would make sure they are done before my appointment so that the consultants had my latest blood results in front of them. And then I moved house. And now my new doctor's surgery refuses to do my blood tests. I have to get them done when I'm at clinic. Eight vials of blood – I'm all black and blue. And I won't get the results of those until my next appointment because they don't volunteer them to be before then."

Patient 3

The concept of Realistic Medicine, first presented by the then Chief Medical Officer as an ambition for NHS Scotland in 2016[7], created an expectation of **shared, personalised decision-making** between healthcare professionals and patients to allow every patient to be a partner in their own health care. While many patients are content to be told what the best treatment for them is, several of the patients we heard from wanted to be more engaged in the management of their PBC.

"Some patients want to know their numbers and a few people ask me for a copy of them. So I'll write the numbers down with the reference ranges and send them in a letter. But there's other people who are simply happy to know if the numbers are okay and get on with their lives. We also discuss things like weight-based dosing of urso, whether they are on the right dose for their weight. I think it is helpful to give some patients the confidence to adjust their dose themselves."

Clinician 5

"I would phone up about the results of my blood tests to be told whether they were within normal ranges. But I started thinking I want a copy of my results. I would like to know what normal is for me rather than simply being told everything is normal."

Patient 2

"I didn't realise until I had a conversation with a wider group of people with PBC that when I was told that my blood results were normal they were actually well off what is normal for everybody else. Why can't I have that as my target and why am I not on a second medication to help me get there?"

Patient 4

Several patients said they would be interested in tracking the progress of their condition with a smart **phone app**, to which their most recent test results could be uploaded. Although the PBC Foundation has an app and there used to be another called UKPBC, none of the patients we spoke to said they currently used an app to support the self-management of their condition.

The case for a single Scottish pathway

At the meeting in the Scottish Parliament to discuss an earlier version of this report, Dr Ruairi Lynch explained that following guidelines to 'treat and stratify risk', 'stage and survey' and 'actively manage' PBC is crucial in patient care.

These, he said, are supported by a 'tick box Bundle' published by the British Society of Gastroenterology that aids healthcare professionals to manage PBC.[8]

However, he reported that a UK-wide PBC audit has shown not everyone is being cared for appropriately, with around 37% of patients underdosed with Urso and only 52% of high-risk patients on second-line therapy; the audit also showing those being treated in a teaching hospital are much more likely to receive second-line therapy than those in a district general.

Dr Lynch said that PBC is a disease that can be easily protocolised and standardised to improve PBC treatment in all hospitals across Scotland. Such a pathway would require GPs to be supported by labs to diagnose people in the community as soon as possible, ensuring patients with cirrhosis or fibrosis receive consistent follow up and complex patients can be referred to the national multidisciplinary team forum to allow consensus to be reached on next steps in their treatment.

A single Scottish pathway – and what should be in it?

In our research, we were told that management guidelines for rare liver diseases exist in some parts of Scotland, and there have been conversations between clinicians about what a 'Once for Scotland' pathway might include.

Asked about what should be in a Scottish pathway, several respondents suggested that a priority must be achieving **better understanding** of PBC across health professions, employers, and the public – and, with better understanding, achieve better diagnosis, care and an end to any lingering stigma.

For the clinicians, it was about **uniformity** in the rates of diagnosis, treatment and care across Scotland – and having the clinical resources to manage every patient properly:

> **"It would be good to have a unified patient pathway, a sort of minimal standard that people can expect if they're treated for PBC, whether they're on an Orkney island or in Edinburgh. The same follow-up, the same access to second-line agents, the same monitoring with FibroScans. And there needs to be equity of access to all that. I don't think that exists in Scotland yet, or in the wider UK either."**
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> **Clinician 6**

> **"It would be good to ensure that we had diagnosis rates that were uniform across Scotland which they're not at the moment. That's not necessarily PBC specific – it's liver care related. We know that there are some boards with very few hepatologists and others with a massive deficit in gastroenterologists per head of the population. The truth is, there is under diagnosis of PBC which is part of a wider picture of a lack of uniform, robust liver care."**
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> **Clinician 3**

> **"Of course, I would like to see everyone in Scotland screened for every single liver disease, though that's not very realistic. But everybody who has abnormal liver biochemistry, particularly alkaline phosphatase, should be tested for PBC specific antibodies and immunoglobulins. There needs to be stratification according to severity and advancement of the condition. I'm a big fan of the liver risk score which is better than the FIB-4 score [**a blood-based diagnostic test that looks at underlying fibrosis**] in PBC patients. What we've learnt from the pandemic is that having a good database is key, so we should be making sure everyone with PBC is on a national database and then we should be diagnosing more people through clever tests like the iLFT."**
>
> **Clinician 1**

"I'd like to see more discussion between professionals because we're going to go from, "there is a treatment," to, "there are a variety of treatments," and it would be really good to have a forum for discussion of what really works in the real world. So, my biggest hope would be that we build on Scotland's autoimmune diseases Multi-Disciplinary Team, that we can deliver care to patients closer to home and that we have the conversations and technology to make that happen."

Clinician 2

"I think the pathway needs to consider itch and other symptomology associated with PBC. And it needs to include a system to refer complex patients to avert them getting referred for transplantation when there may have been opportunities to intervene earlier."

Clinician 4

For patients, there was a hope that any pathway would give equal priority to identification and treatment of symptoms as to interventions that seek to arrest damage to people's livers. Patients also expressed the hopes that they could be seen by the same healthcare professional throughout their journey, and that they could become more involved in monitoring their own health.

"Discussion of symptom management should be just as important as disease progression in clinical appointments so that patients feel heard. And every patient should be able to be part of the community where they can speak to other patients who understand, who could make it much less lonely."

Patient 5

"It's about consistency – because if you're seeing different clinicians all the time it's not good for the patient and it's not good for that clinician's duty of care to that patient. So, a quicker diagnosis and for the patient to be heard, for them to be able to ask 'what happens next?'"

Patient 3

"Any pathway must include time to explain exactly what's going on to every patient, letting them know what their results are, discussing why a particular number might be high, what does it mean for me, telling me what path my disease is taking. And it must include talking about stages. I understand that might complicate things and worry some people, but nobody seems to talk about stages of this condition."

Patient 2

Thoughts for the future

Several clinicians talked about the recent increase in the number of clinical trials for possible treatments when looking to the future:

"I think having more second-line therapies that are well-tolerated, that have better side-effects and, ideally, improve the quality of life and the symptoms that go with PBC, that would be a significant step forward."

Clinician 3

Several clinicians talked of the need to introduce the iLFT across Scotland.

Another looked forward to research being undertaken into finding biomarkers to identify patients most at risk of their PBC progressing – possibly by employing artificial intelligence and machine learning to find common factors in the test results of people whose PBC is most severe.

For one patient, the ambition for the future was straightforward:

"My hope is for a cure for PBC. There's a lot of research going on around it. A lot is happening in terms of clinical trials for PBC at the moment not just for treatments that address progression but also for symptom management, which is massive."

Patient 5

5. Contributors

We are very grateful indeed for the time and help given to us by:

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- **Dr Andrea Broad** Consultant Gastroenterologist and Hepatologist, NHS Highland.
- **Ms Mhari Brotherston** PBC patient.
- **Ms Mo Christie** Head of Patient Services, PBC Foundation; PBC patient.
- **Professor Jonathan Fallowfield** Chair of Translational Liver Research at University of Edinburgh; Honorary Consultant Hepatologist, NHS Lothian.
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- **Dr Mathis Heydtmann** Consultant Gastroenterologist and Hepatologist, NHS Dumfries & Galloway and NHS Greater Glasgow & Clyde
- **Dr Ruairi Lynch** Consultant Hepatologist and Gastroenterologist, NHS Tayside.
- **Dr Jo McCardle** PBC patient.
- **Ms Gill Morton** PBC patient.

Please note: the numbers assigned to the contributors do not correspond with the order in which the contributors are listed here.

Appendix 1: Glossary

alkaline phosphatase
An enzyme.

bezafibrate
A fibrate drug used as a lipid-lowering agent to treat high cholesterol. Used off-licence in the treatment of PBC.

Centre for Sustainable Delivery
A national unit hosted by NHS Golden Jubilee and commissioned by the Scottish Government, to drive NHS recovery, and renew and transform Scotland's health care system through advising on innovation, collaboration and clinical leadership.

Cirrhosis
Scarring of the liver caused by long-term liver damage.

Fibrosis-4 (FIB-4)
A non-invasive scoring system to estimate the amount of scarring in the liver.

FibroScan®
A type of ultrasound to measure liver inflammation and scarring.

Fibrosis
The formation of a large amount of scar tissue in the liver, when it attempts to repair and replace damaged cells. Severe scarring can result in cirrhosis.

GPs
General Practitioners.

intelligent Liver Function Test
(iLFT) Augmented Liver Function Test (see appendix).

Liver Function Test
A group of blood tests to assess healthy liver function.

Liver risk score / LiverRisk score
A prognostic scoring system using eight variables to predict risks of and from cirrhosis.

MDT
Multi-Disciplinary Team.

MSP
Member of the Scottish Parliament.

Naltrexone
An opioid receptor blocker.

NHS National Servies Scotland
A national NHS board providing central support a range services for NHS Scotland regional boards.

NHS Inform
Scotland's national health information service

Obeticholic acid
(OCA) A synthetically modified bile acid and potent agonist of the farnesoid X nuclear receptor (FXR) that is used to treat liver diseases.

Pruritus
Itch.

Rifampicin
An antibiotic.

UDCA
Ursodeoxycholic acid, sometimes shortened to 'urso'.

Appendix 2: Intelligent Liver Function Testing (iLFT)

In Tayside, a GP can request an Intelligent Liver Function Test (iLFT) for patients they believe may be at risk of liver disease or have abnormal liver function tests.

When submitting their samples, GPs input additional details about their patient, stating whether they drink more than 14 units of alcohol a week and which BMI range they fall into.

Abnormal results for a sample put through the standard liver function test will then, in around 60% of cases[9], reflexively undergo the full cascade of further tests to check for other conditions[10].

The outcome of the second set of tests, when combined with the personal details of alcohol consumption, BMI and any existing diagnosis of metabolic syndrome, are fed into an algorithm that creates a report to confirm one or more of 33 different diagnoses. The report includes a three line summary and a link to a more detailed one page, giving the most likely diagnosis and an assessment of the likely level of fibrosis – along with a proposed management plan for that patient, identifying:

1. Those patients requiring to be seen in a liver clinic, specifically those with PBC, autoimmune hepatitis (AIH), Hepatitis B or C infection, metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol related liver disease (ARLD) who might have fibrosis;

2. Those who need assessment in a medical or nurse-led clinic;

3. Those with MASLD/ARLD without fibrosis who can be manged in Primary Care;

4. Those without a clear diagnosis for whom further evaluation is required; and

5. Those who have jaundice who need to be fast-tracked to a jaundice clinic.

In Tayside, iLFT now generates some 90% of referrals into liver clinics. A study comparing the number of patients identified in the region before and after the introduction of iLFT five years ago is underway. While the automated system means there is little additional time for laboratory staff, immunologists and biochemists have an increased number of cases to review.

In 2021, a University of Dundee team reported that:

> **'iLFT increases diagnosis of liver disease by 43%, with diagnostic accuracy over 90% and enables earlier identification of treatable liver disease. It makes standard care easier and is estimated to deliver cost saving to the NHS of £3,216 per patient lifetime compared to current ideal investigation. A single sample provides results which would previously have required up to six separate bloods which reduces GP contacts by an estimated 60%.'[11]**
>
> **News Release**

The clinician respondents were all supportive of having access to iLFTs but their views on how close they felt the system was to being introduced in their local service varied depending on the health board they work in.

> **"GPs, on the whole, love it because it makes it clear what to do. In the past, some abnormal LFTs weren't acted upon, and this has changed that."**
>
> **Clinician 4**

"There are some teething problems with regards to the lab IT systems needing to be adapted for it. We're getting a new lab system and, in the meantime, programming it into the old lab system is simply too costly for most health boards."

Clinician 1

"We have been talking about that in [our board area] for a long time, but we don't have the correct hardware. The hardware used in the laboratories here is not compatible with the platform that's currently used for iLFTs. I think reflexive testing is interesting. It is supposed to be more efficient, but I have some reservations. Maybe more people would come through via that route."

Clinician 6

"Last year's big investment was putting the right machines in. So we now have the machines that could do those things. This year we are getting everything calibrated. Primary care now has electronic requesting. So we have spent the last year or so putting the building blocks in place that you would need to be able to introduce iLFTs".

Clinician 2

Endnotes

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