FARSITE takes clinicians one step closer to integrated diagnostics for liver disease

Supporting early diagnosis of liver disease

ID LIVER[1] is a three-year clinical trial led by The University of Manchester and Manchester University NHS Foundation Trust in partnership with The University of Nottingham, Nottingham University Hospitals NHS Trust, global industry partners Roche Diagnostics and GE Healthcare, and SMEs including NorthWest EHealth (NWEH). It is funded by the UK Government's Innovate UK Industrial Strategy Challenge Fund. The project began in 2020 and builds on established research into biomarkers associated with liver disease.

Dr. Varinder Athwal

Dr. Varinder Athwal is a consultant clinical hepatologist at the Manchester University NHS Foundation Trust and a University of Manchester Senior Lecturer. Dr. Athwal's PhD and research interests include biomarkers of liver disease and mechanisms of liver fibrosis. Dr. Athwal is a previous NIHR Clinical Lecturer and Clinical Research Training Fellow with the Medical Research Council (MRC).

Dr. Huw Purssell

Dr. Huw Purssell is a gastroenterology registrar working in the North Western Deanery and is currently working as a clinical research fellow at Manchester University Hospitals NHS Foundation Trust. Dr. Purssell is also the ID LIVER Clinical Research Fellow and presents the findings and impact on the clinical community of the study at events across the UK.

Oliver Street

Oliver Street is the ID LIVER Project Manager, uniting the team of university researchers, NHS professionals, and industry partners from across the UK to address a major healthcare challenge. The study sets out to develop a novel liver disease diagnostic pathway, which will allow for an earlier, more accurate, and potentially life-saving diagnosis.

When early diagnosis is critical

Society's current inability to identify liver disease early means that a calculated and patient-specific risk analysis is critical to producing an early diagnosis of the condition.

By using FARSITE technology from NWEH, which integrates patient risk factors, biomarkers and diagnostic data, the Integrated Diagnostics for Early Diagnosis of Liver Disease (ID LIVER) study aims to identify patients with early-stage liver disease and those at risk of progressive life-threatening liver disease, including liver cancer.

It is hoped that as a result, a new diagnostic pathway for the NHS will be defined that could be replicated and upscaled in other parts of the world or other areas of healthcare.

"Our overall goal is to change clinical practice, and to set up a service where patients who have chronic liver disease risk factors are assessed almost automatically. This important project may not have got started without the early support of NorthWest EHealth."

Dr. Athwal, Honorary Lecturer, Teaching & Research, University of Manchester

Spotlight on FARSITE

Liver disease:
a silent killer

Chronic liver disease (CLD) is a leading cause of both mortality and morbidity in the UK and, along with heart and respiratory disease, is in the top three for inequitable healthcare.[2] While almost four in ten people are at risk of liver-related health problems, the majority are only diagnosed at late stages, leaving very limited options beyond transplantation – or premature mortality.

"It's a tragic truth, but unfortunately by the time most people know they have liver disease it is far too late," says Dr. Varinder Athwal. *"They present at A&E with jaundice or symptoms of liver cancer, when prognosis is very poor. We need to see them much sooner, because then we can actually do something about it."*

Dr. Athwal adds, *"At earlier stages, it can be pure luck that patients see a doctor or clinician, perhaps because they've come in to have a blood test or diabetes check, or even for something relatively minor such as a fungal toenail infection. We can no longer afford to detect liver disease purely by serendipity."*

There is currently no single diagnostic test that can identify when the disease begins to develop, plus, as Dr. Huw Purssell points out, only five percent of abnormal liver tests actually correspond with having liver disease. *"GPs are forced to refer reactively,"* he says. *"There is no clear pathway for patients who potentially have a liver disease diagnosis."*

If caught early enough and with lifestyle modifications, it can be possible to reverse liver-related health problems. Therefore, more accurate assessment and timely diagnosis is needed for reversal of CLD. Dr. Athwal and his colleagues at the University of Manchester are addressing this issue as part of the ID LIVER project.

Facilitating early detection

ID LIVER is a Manchester-led research project with three key aims:

- Facilitating earlier detection of liver problems in the community
- Assessing whether MRI scans reduce the need for invasive liver biopsies
- Identifying those patients who are at risk of developing liver cancer earlier

Early identification and assessment of people with risk factors and improving the process is critical. Dr. Athwal comments: *"We're using currently available technologies and novel biomarkers to see if they can actually tell us earlier on if someone has the potential to develop liver disease."*

As part of this pragmatic clinical trial, patients identified as being at risk of liver disease attend a liver health check screening. A non-invasive FibroScan ascertains the stiffness of the liver, which helps identify scarring. Blood samples are taken from patients who agree to be part of the study, which the researchers will then analyse to compare biomarkers and liver scarring. The team, in collaboration with Jiva.ai, will then use the compiled medical data to develop, train and validate a risk prediction tool, powered by artificial intelligence, to predict the risk of clinically significant liver disease and disease progression.

"The reason we established ID LIVER was because we wanted to develop new patient pathways, pathways that were so straightforward that they can easily be adopted," adds Oliver Street. *"Our overall goal is to improve clinical practice, and to set up a service where patients who have a higher risk of liver disease are identified and assessed at an earlier stage and given the appropriate care."*

Lucinda Osbourn, Senior Delivery Manager at NWEH, highlights that this is not a typical clinical trial. *"It's all about introducing a new pathway within the NHS."* Nor is it a profit-making initiative. *"We know that the North West has a significant morbidity,"* says Dr. Purssell. *"So this is us trying to help people in the local community who have risk factors and could go on to develop liver disease – if they're not diagnosed early enough."*

A set of clinical challenges

Issues with CLD diagnosis have been compounded during the COVID-19 pandemic. Public safety concerns meant that the number of patients attending appointments was restricted, reducing even further the already slim potential for identifying CLD.

This impacted directly on ID LIVER; in particular the ability for real world recruitment and the conducting of clinical trials. Firstly, it limited contact with potential patients, which started to delay recruitment by months. *"For clinical trials, it is so important to have a range of ages, genders, ethnic groups and socioeconomic backgrounds,"* says Osbourn. *"We needed to find a new solution to patient recruitment."*

Secondly, it required collaboration with GPs who are still struggling with unprecedented workloads. *"Getting overworked GPs involved at a time when they were trying to administer COVID and flu vaccines – not always onsite – was understandably very challenging,"* says Osbourn. *"They have had no bandwidth to even do a relatively small amount of additional work. It meant we had to give our methods serious consideration: giving any more work to primary care would have meant no one would actually want to be part of the project – and we needed their support."*

Enter FARSITE

FARSITE allows teams to identify patients across GP practices with specific risk factors and a set of inclusion and exclusion criteria. And although recruitment for clinical trials is often challenging and time-consuming – depending on the demographics of local communities, engagement level of GPs and technological infrastructure – NWEH's FARSITE technology, according to the ID LIVER team, has simplified and sped up the process.

"In this case, we gave NWEH a list of risk factors, such as obesity, alcohol consumption, diabetes, and so on. From there, via FARSITE, we were able to target practices with patients who met the number of risk factors and were therefore eligible for the study," says Dr. Purssell. It also delivered the wide-ranging patient demographic the team required. *"NWEH has both the technology and the footprint in Greater Manchester for us to have the reach that we needed,"* adds Dr. Athwal.

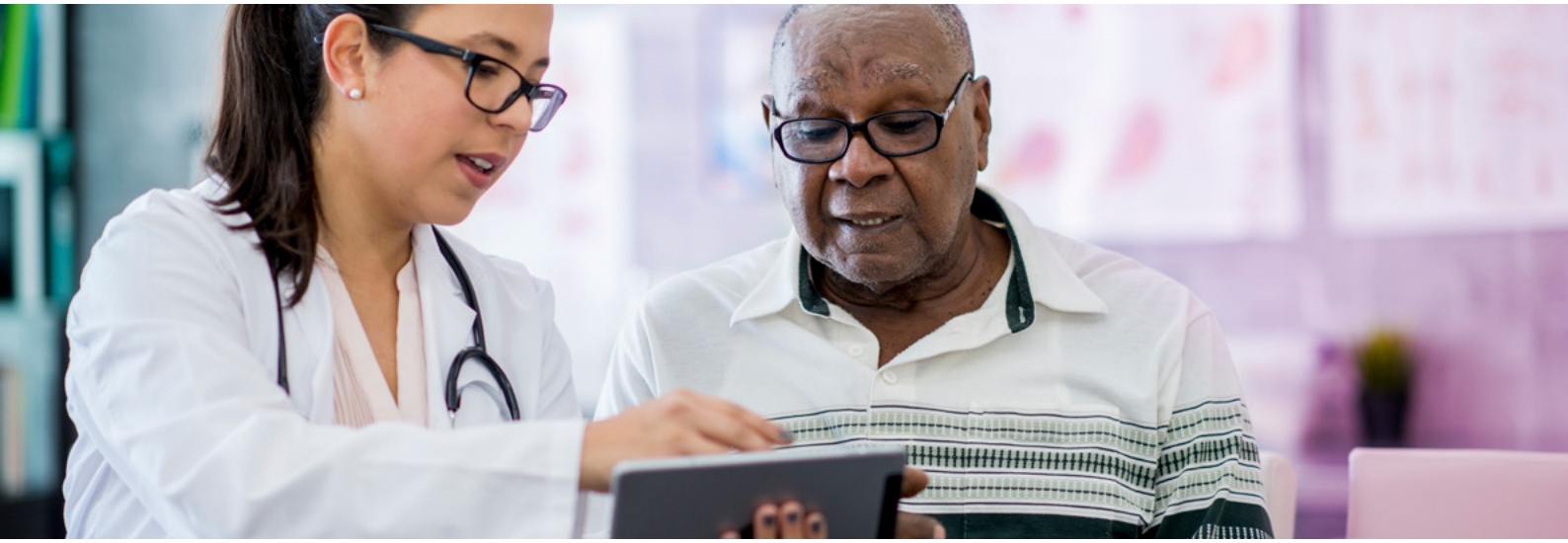
The team was also able to adjust the exclusion criteria throughout the recruitment. *"We certainly changed some criteria partway through to make sure the patients we were seeing were appropriate,"* says Dr. Purssell. *"For example, we said we didn't want to see anyone who it would be inappropriate to see, such as those with a palliative diagnosis. NWEH made that process incredibly smooth for us and for the GPs involved."*

At this stage, if GPs at the practices were willing to take part, they simply needed to confirm that letters could be sent to the relevant patients to invite them for a liver health check. *"It requires minimal effort and time from the GP sites,"* says Osbourn. *"The benefit of using FARSITE is that we can run searches and share directly with GPs, without having access to any identifiable patient information. After obtaining appropriate approvals, they simply select who they want to send the letters to."*

Dr. Athwal adds: *"NWEH gave us the tools to absolutely minimise the workload of the GPs, and that's been really critical to the success of this project. Also, a lot of GPs had used FARSITE in the past, so knew how it worked. They were reassured it wouldn't add to their already considerable workload, so were much more willing to support us in our research."*

Dr. Athwal says that without NWEH, the team may have struggled, particularly at the height of the pandemic. *"This project may not have got started without the early support of NWEH – and they were very good at getting everything over the line for us."*

He valued both the time-saving and the minimal financial impact. *"Without NWEH, we would have had to employ somebody to go through the primary care records manually to look for risk factors. That would have been incredibly time consuming and very expensive."* And as he points out, cost plays a huge part in uptake from the NHS. *"Commissioners quite rightly have to care about hard data points: will it save money? Does it lead to better health outcomes? FARSITE has given us the tools and real-world data to prove both."*



Real world delivery

"The aims and objectives of the project were initially to recruit from three GP sites within the Greater Manchester region," says Osbourn. *"The intention was to get as many patients through the pathway and gather enough data points to allow us to analyse and ultimately produce a pathway and a recommendation to the NHS."*

Patients have currently been recruited from five sites, with potential for more. *"We've thus far recruited more than 1,000 patients, against a target of 1,200,"* says Dr. Athwal. *"Our plan was to meet that target by August 2023, but we're going to hit that much earlier, in the first quarter of 2023."* Due in the main to ID LIVER, the North West is now one of the highest areas for liver disease research recruitment in the UK.

The ID LIVER team plans to embark upon another phase of this project, to prove and demonstrate the proposed pathway on a wider scale. Ultimately, they hope to roll out the project as the standard clinical pathway across Manchester.

"We're waiting to hear the outcome of another award grant," says Dr. Athwal. *"If that is successful, this could become the de facto method of finding and assessing people for liver disease for 2.5-3 million people across Greater Manchester."*

Crucially, the success and ease of recruitment has provided demonstrable benefits to GPs.

"The GPs we've spoken to have been really engaged, and think that what we're doing – making this opportunity available for patients in the community, and trying to improve the pathway and diagnosis of liver disease – is extremely positive," says Osbourn. *"We are helping GPs to identify patients within their practice who meet the criteria required for clinical trials – ultimately helping to deliver better health outcomes. It is undeniable that one of the selling points has been the ease of use of FARSITE and the support of NWEH."*

Upscaling
and beyond

In a broader sense, the project focuses on community diagnostics and integrated care systems – which, Dr. Athwal says, is at the heart of the NHS 50-year plan.

"As much as our work might be focused on liver disease, it is multimorbidity that is the disease: for example, a patient's diabetes and their heart risk, as well as their liver," he says. The team's identification of risk factors is allowing them to identify people with multimorbidity. *"This method has the potential to be scalable and an efficient way of carrying out multiple assessments – blood pressure, diabetes care – at the same time. Imagine if we could state that 90 percent of people assessed don't have and are never going to have a particular disease, so we just need to focus on this 10 percent. It could change patients' lives and deliver ground-breaking new efficiencies to clinical practice in the UK."*

NWEH

Spotlight on FARSITE

The NWEH Feasibility Assessment and Recruitment System for Improving Trial Efficiency (FARSITE) is an established feasibility tool to search, find, and recruit participants from primary care settings into clinical trials, whilst still preserving their confidentiality. The technology suite permits rapid and accurate protocol design, meaning processes that may have taken weeks to months can now be achieved in hours or days, while ensuring accuracy, diversity of patient recruitment and ease of use.

True-to-life clinical trials

NWEH provides the pharmaceutical industry with a holistic approach to clinical trial design and delivery, helping bring drugs to market faster. FARSITE has the potential to streamline the complex processes associated with conducting trials in a regulated environment, affording the opportunity to bring life-saving therapeutics to the market quickly and efficiently.

NWEH is a leading figure in the field of electronic health record (EHR)-enabled randomised clinical trials. NWEH built the technology behind the success of the pioneering Salford Lung Study and is the only organisation in the world to have evaluated the safety and effectiveness of a pre-licence medicine in a real-world setting.

From feasibility studies and trial design to clinical delivery and data analysis, NWEH supports the success of pharmaceutical companies and contract research organisations across the globe.

To find out more about the NWEH true-to-life approach to clinical trials and how the company's tools and expertise in recruitment, design and feasibility, clinical management and delivery, safety data reporting, and data analysis could be applied to future projects, visit nweh.co.uk.

NWEH WEBSITE

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This case study has been independently authorised by NWEH.

References

[1] L. Bennett, H. Purssell, O. Street, K. Piper Hanley, J.R. Morling, N.A. Hanley, V. Athwal and I.N. Guha, Health technology adoption in liver disease: innovative use of data science solutions for early disease detection, Front. Digit. Health, 2022, 4:737729, doi: 10.3389/fdgth.2022.737729.

[2] Health profile for England: 2018. Public Health England, London (2018).

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