Pioneering clinical trial model using FARSITE from NWEH supports major study into inflammatory bowel disease

The study is a collaboration between NorthWest EHealth (NWEH), National Health Service (NHS) England and one of the world's leading biopharmaceutical companies. The sponsor chose to partner with NWEH on this project because of its pioneering clinical trial technology which facilitates patient recruitment and streamlines data analysis.

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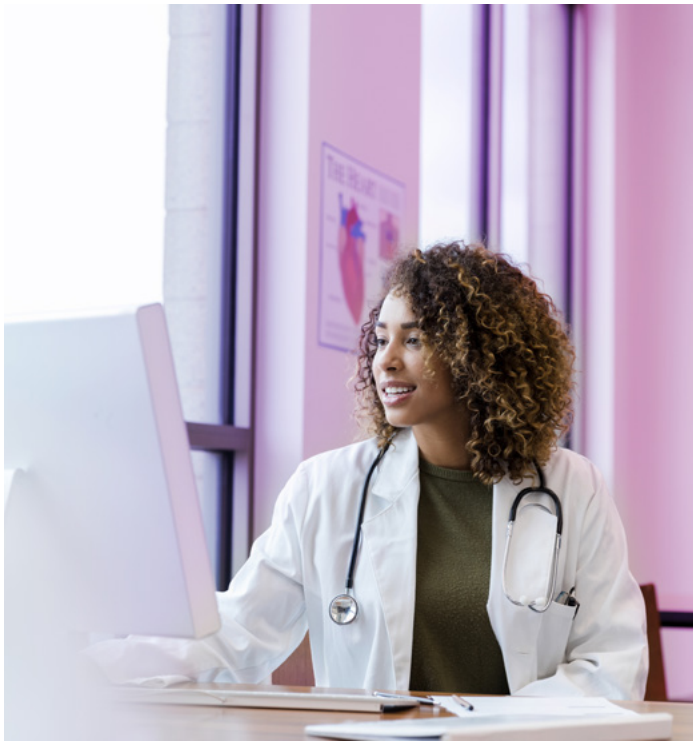
Current evidence shows there is an unmet need for accurate and up to date prevalence data of inflammatory bowel disease (IBD) in the psoriasis (PsO) population.

However, previous studies have relied on diagnosed IBD only, and have failed to assess the prevalence of clinical characteristics or symptoms strongly indicative of IBD. In this case study, we talk to several representatives from NWEH about the EPIC study into the connection between PsO and IBD, and the drivers, challenges and advantages of running a real-world clinical trial designed to improve diagnostics and patient care in the primary care setting.

"This project is an example of the partnership approach envisaged by the UK Government's Life Sciences Industrial Strategy, which stresses the importance of collaboration to generate real-world evidence, expand our collective knowledge of disease and ultimately work together to raise standards of care. We hope that the partnership model we have developed with NWEH could serve as a best practice exemplar for future industry-NHS collaborations."

Sponsor



Spotlight on FARSITE

A clinical challenge

IBD is a chronic inflammation of the small intestine or colon, and results from a weakened immune system.

Recent evidence suggests a high correlation between IBD and PsO, a skin condition also thought to be linked to immunity; although the exact causes are unknown, it has been suggested that it could be triggered by intestinal microbiota and loss of tolerance at gut and skin level.[1]

Currently, PsO patients are not routinely screened for IBD, and it is not yet known how prevalent the presence of IBD red flags or raised faecal calprotectin are in cases of moderate-to-severe PsO.[2] Previous studies have relied on diagnosed IBD only and have failed to assess the prevalence of clinical characteristics or symptoms strongly indicative of IBD. Understanding the link between these two illnesses – and specifically, how psoriasis could signify IBD – could facilitate earlier diagnosis of IBD in patients and allow for more tailored therapeutics,[3] as well as understanding more about the mechanisms of the immune system.

It is acknowledged that more research into the link between IBD and PsO is needed. It is impacted, however, by general difficulties around the recruitment and retention of participants for clinical trials. Difficulties in recruitment can pose *"Serious threats to both the internal and the external validity of a research study."*[4] There is a widely held belief that the industry has *"A long way to go before it can claim to be truly patient-centric,"* and that *"A shift in attitudes, as well as greater steps to involve the patient voice, will be needed."*

These existing challenges in improving clinical trial recruitment have been compounded by the COVID crisis. Restricted access to primary care centres, staff shortages and increased workloads have placed additional pressure on clinical research.

"COVID didn't stop us from receiving samples or delivering the protocol," says Verity. *"But it did initially stop us from recruiting more patients, to then be able to enrol them and obtain the samples we needed."*[5]

In the case of the EPIC study into the prevalence of IBD in PsO patients, the use of the NWEH Feasibility Assessment and Recruitment System for Improving Trial Efficiency (FARSITE) and ConneXon technologies allowed the EPIC team to drive the research forward despite the challenges.

"COVID meant we really had to re-evaluate our processes and change how we managed the study," adds Verity. *"Using our pioneering clinical trial model allowed us to manage patients in a multidisciplinary way even during the pandemic, and meet our recruitment targets."*

A unique study

The EPIC study, which commenced in 2019, is a collaborative project driven by a committee comprising UK gastroenterologists, dermatologists, biostatisticians and GPs, alongside a sponsor and NWEH.

The primary aim of the study is to determine the combined proportion of diagnosed IBD, raised faecal calprotectin and IBD red flags in the moderate-to-severe psoriasis population, before characterising the patients in these populations and describing their management in the 24 months following enrolment.

First, adult patients with moderate-to-severe PsO were recruited from 12 primary care practices in Greater Manchester, between November 2019 and April 2021. In these patients, a prior diagnosis of IBD was confirmed using a retrospective review of primary care medical records. For patients without a confirmed IBD diagnosis, faecal calprotectin (FCal) monitoring and a bespoke questionnaire derived from validated measures of gastrointestinal (GI) symptoms and IBD red flags (CalproQuest IBD and Red Flag Index) were used to screen for IBD risk.

“This study was interesting not only from a data analysis perspective but also because it involved collaboration with a multidisciplinary team including autoimmune disease area experts, gastroenterology and dermatology,” says Dr. Migas. The team was asked to look for a wide variety of associated comorbidities, such as rheumatoid or psoriatic arthritis, coeliac disease, lupus, diabetes, mood disorders and general cardiovascular issues.

The study is also unique in that patients were recruited from a primary, rather than a secondary care setting. “Using FARSITE to access real-world electronic healthcare records (EHRs) from a primary care setting has allowed us to recruit a much more diverse patient population,” says Williams. “That means, therefore, that the results of this trial will be much easier to generalise.”

In collaboration with the trial sponsor, the following key tasks were identified:

- Identification of eligible patients from primary care centres across Greater Manchester using NWEH's FARSITE tool
- Protocol and Statistical Analysis Plan writing with input from medical experts
- Ethics application and Research Ethics Committee (REC) annual report submission carried out by NWEH regulatory expert
- Site activation support and confirmation that principal investigators (PIs) can fully execute protocol
- Study recruitment and delivery monitored by NWEH nurses and study administrators
- Study compliance and quality assurance carried out by regular monitoring visits performed by a NWEH clinical research associate (CRA)
- Study relevant medical records being captured in ConneXon, the bespoke NWEH electronic case report form
- Data analysis, interim and final reports being performed by NWEH's data scientists and statisticians
- ·Study archiving to be carried out by NWEH.

Interim results show that 3.6% of patients in this cohort with moderate-to-severe PsO had a confirmed IBD diagnosis.[6] Further, approximately two-thirds of patients exhibited at least one indicator of IBD risk. The researchers stated in the published paper that these results support further investigation and assessment at the 24 month stage.

A 360-degree service

The NWEH's FARSITE platform provided the researchers with the technology to monitor the whole process, from inception to delivery.

"It was what I would call a 360-degree service, allowing us to confirm feasibility and providing us with everything we needed right through to the delivery of the protocol and the write-up at the end," says Jo Verity. *"FARSITE was without a doubt one of the key enablers."*

FARSITE is designed to accelerate the patient recruitment process. *"We were working with 23 different sites, which demanded a lot,"* says Verity. *"We needed to keep track of how many patients returned their samples and how many returned their questionnaires. We had to chase up patients who missed a follow-up for whatever reason, consider the quality of the data, and look at any protocol deviations. Keeping to our timelines was tough because of the pandemic. But ultimately, using FARSITE helped us achieve as high a recruitment as possible."*

Dr. Migas agrees: *"We utilised ConneXon to make sure we'd collected suitable information from patient medical records, as well as study specific data points like laboratory results and questionnaire answers,"* Dr. Migas says. *"With electronic case report forms (eCRF), all the data is collected in one place, and this integrated data system, supported by data management and quality services, allowed us rapid and effective analysis; in fact, the first round of results at the interim stage was delivered within 2 weeks. It was an extremely efficient, robust and quality-assured process."*

At the early stages, a pilot study was conducted by the EPIC committee to prove the effectiveness of the FARSITE technology. *"It was a feasibility study, where we used FARSITE initially to check that we had the appropriate patient population,"* says Williams. *"We weren't sure if the system would allow us to actually find patients with moderate-to-severe psoriasis, and we needed to become very clear on the proxies we'd need to use to identify those patients."*

This pilot study proved the principle that the population for the trial would be appropriate and that it would allow the EPIC team to generate more generalisable, traditional clinical trial data. *"It really enabled us to drive the protocol design and definitions."* says Williams.

A model of best practice

The Life Sciences Industrial Strategy provides recommendations to the government on the long-term success of the life sciences sector.

These include: *"improving the UK's clinical trial capabilities so that the UK can best compete globally in our support for industry and academic studies at all phases."* As a strategic goal, the report also suggests:

"A 50% increase in the number of clinical trials [...] and a growing proportion of change of practice and trials with novel methodology. [...] In the next five years, the NHS should engage in fifty collaborative programmes in late-stage clinical trials, real-world data collection, or in the evaluation of diagnostics or devices."[7]

The sponsor states in a press release that the collaborative approach of the EPIC committee allowed improved ways of working and protocols to be developed: *"This project is an example of the partnership approach envisaged by the UK Government's Life Sciences Industrial Strategy, which stresses the importance of collaboration to generate real-world data. Harnessing the power of NHS data sets offers a significant opportunity to expand our collective knowledge of disease and ultimately work together to raise standards of care."*

A key opportunity

The NWEH team believes that EPIC has shown a need for further investigation into the connection between inflammatory disorders, beyond IBD and PsO.

"It has already been shown that those with psoriasis are at risk of developing bowel problems because of that auto-immune response," says Dr. Migas. "The question is: does it affect other organs other than the skin? There may be more issues that patients are suffering from that are not as visible."

Dr. Migas hopes that the team's work will help others studying in related fields. *"Our expertise in real-world evidence and the FARSITE and ConneXon platforms offers a fantastic opportunity for other researchers to utilise our skills and knowledge."* She says that the structure of the project will make it easier to collaborate. *"We are not overwhelmingly large and, thanks to our technology, our processes are efficient, with a strong emphasis on data quality and integrity, which means we can get reliable answers quickly."*

The broader impact both of the study itself and the way the trial was conducted will depend very much on the results, Dr. Migas says. But the key beneficiaries, she says, are the patients themselves: *"At some point in the future, this could mean patients receive more aligned, joint treatment in cases where there is pathophysiology from more than one illness. Ultimately, we are hoping to improve care from the patient perspective."*

Best practice in feasibility

NWEH's FARSITE platform is an established feasibility tool to search, find, and recruit participants from primary care settings into clinical trials, whilst still preserving their confidentiality. In this study, the platform was used to recruit patients from 12 primary care practices in Greater Manchester.

Increasing patient safety

The NWEH ConneXon clinical trial platform provides a secure, validated and modular system built to accelerate trials whilst increasing patient safety. ConneXon comprises a full electronic data capture (EDC) system, with data capture directly from source, plus a configurable electronic case report and a close to real-time safety monitoring system. This, together with parallel delivery of data for effectiveness and efficacy, allows the platform to be configured to the needs of each individual study. In this trial it is being utilised for data collection and remote patient safety monitoring with minimal intervention, thereby reducing patient visits and maintaining real-world conditions for participants.

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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, 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 around the globe.

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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 authored by NWEH.

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