CHIEF SCIENTIST OFFICE

CODE: ETM/414

RESEARCH PROJECT BRIEFING

The ScOttish Psoriatic artHritis Observational Study (SOPHOS)

AIMS

The main aim of the SOPHOS study was to create a national inception cohort and biobank of patients with a new or recent (within 4 years) diagnosis of psoriatic arthritis (PsA) in order to address a range of clinically relevant questions. Approximately 2-3 in every 10 people with the common skin condition psoriasis will also develop PsA. Most studies in PsA have focused on patients with established disease who have had this condition for many years, making it difficult to distinguish the immune changes of the underlying inflammatory PsA condition from those due to previous treatments or the long-term consequences and damage from the condition.

A main aim of SOPHOS was to identify key combinations of molecules ("molecular signatures") associated with the various patterns of the disease, in order to better understand these processes and how they may be treated, as well as to see if these molecular signatures predict future progression of the disease and response to therapies.

KEY FINDINGS

300 patients with new or recent onset PsA were recruited and found to have a high burden of obesity and a range of clinical manifestations that differ from those seen in cohorts of patients with established PsA. Work is still ongoing to establish how these link to the underlying molecular signatures.

Preliminary analysis has identified potential epigenetic and molecular biomarkers that may help predict whether or not a person with PsA will respond to treatment with methotrexate, the most widely used first line therapy.

A significant majority of patients with early PsA would not meet the inclusion criteria for randomised controlled trials used for testing and licensing of the therapeutic agents used in clinical practice. However, PsA has a major impact on patients even in the early stages and only about a third of patients in our cohort achieved low disease activity states with standard NHS treatments.

WHAT DID THE STUDY INVOLVE?

SOPHOS was an observational (no intervention as part of the study) cohort and clinical laboratory study run across multiple centres in Scotland. Adult patients attending secondary care rheumatology clinics across Scotland with a new diagnosis or an existing diagnosis of PsA within 4 years (early) were invited to participate in the study. The 300 consenting participants underwent standardised data and blood sample collection every 6 months for 2 years. Collected data included demographics, comorbidities, detailed PsA specific clinical assessments, including disease activity overall and across a range of domains, as well as patient reported outcomes, including pain, fatigue and the impact of the disease on their quality of life. In addition to routine NHS tests, blood and urine samples were also collected, processed and stored (biobanked) using robust standardised operating procedures. Recruitment and analysis were delayed by the COVID pandemic when patients were not seen routinely in clinics, so some later follow up visits were done remotely.

In addition to our ongoing analysis directly addressing the main study aims, data and samples are available for other researchers to access to address other scientifically and clinically relevant questions. Samples and data are already contributing to the EU IHI HIPPOCRATES PsA consortium bringing together academic researchers (Glasgow are a key partner), industry partners and patients from across Europe to address the key challenges in PsA. This consortium will also allow us to expand and validate some of our findings in SOPHOS in our groups of patients with PsA.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

300 participants with PsA were recruited of which 180 had a new diagnosis of PsA and 120 had a recent diagnosis (within 4 years of diagnosis). Overall, 54.7% were female with a mean age of 47.2 years. The mean body mass index was 30.3 kg/m , with 80% categorised as overweight or obese. 15.7% were current smokers at the time of recruitment.

Patients had skin psoriasis for a median of 15.5 years by the time of PsA diagnosis and some musculoskeletal symptoms for a year before presentation, suggesting there are opportunities to identify and treat patients earlier. 83% of participants had current skin psoriasis at the time of recruitment although this was mild in the majority. All key comorbidities were more common in participants with recent diagnosis than those with new diagnosis, suggesting these accrue over time in PsA and raising the possibility that interventions in early disease may help prevent these.

Participants had a median of 2 swollen and 2 tender joints at the time of presentation – most patients with new/recent onset PsA would therefore be excluded from standard phase 3 clinical trials used for licensing of new drugs. Even at presentation and in early diseases, PsA has a major impact on patients in multiple domains. Symptoms and impact were generally higher in those with new onset of PsA but patients with existing early disease still had significant symptoms and impact of their disease. At any specific study time point, only a third of participants fulfilled minimal disease activity criteria.

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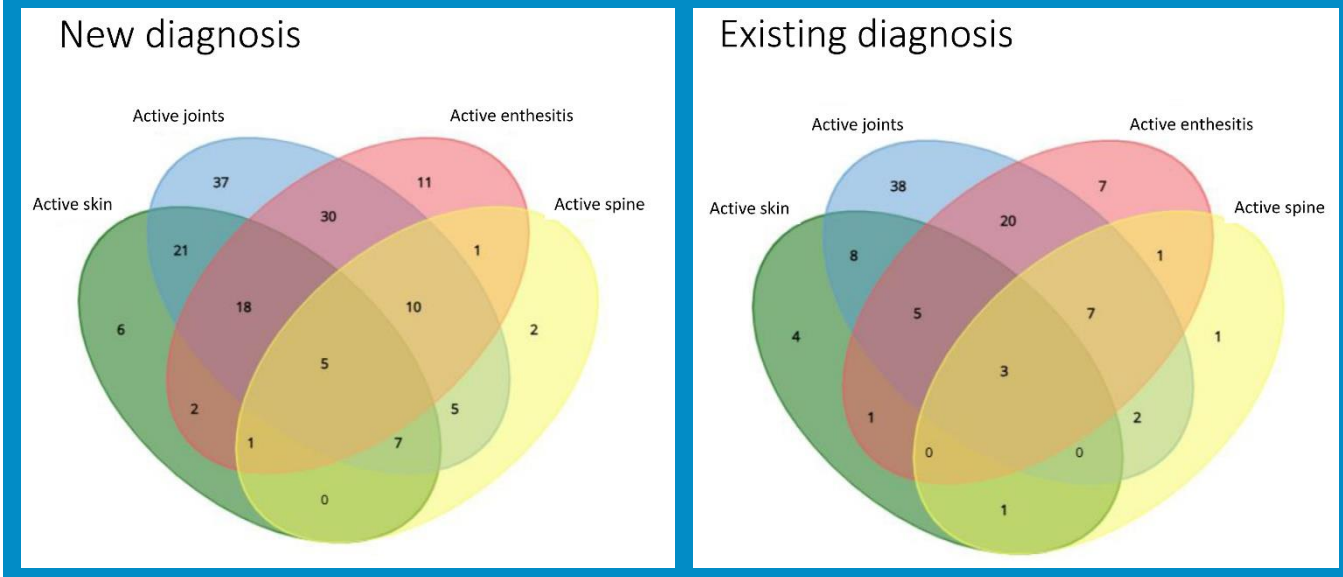
There is significant heterogeneity in PsA even at diagnosis. An example figure of the complexity of involved domains in those with new and recent diagnosis is shown in Figure 1. Analysis is ongoing to evaluate whether and how these patterns are associated with a range of metabolic, epigenetic and protein biomarkers in blood.

We have also identified potential epigenetic biomarkers (chromatin conformation signatures) and metabolites that may predict response to methotrexate, the first therapy typically used in PsA. These are being tested further in SOPHOS and will then be validated in other cohorts to assess if they also predict treatment response in these patients. If confirmed and validated in other cohorts, this could lead to biomarkers that help identify patients who are likely to respond well to methotrexate, justifying early use, and those unlikely to respond to methotrexate, supporting bypassing methotrexate and moving straight to an alternative therapy.

Figure 1: Number of participants with specific phenotypes



WHAT IMPACT COULD THE FINDINGS HAVE?

This information will help lead to a better understanding of this complex condition, especially in its early stages, how it impacts patients and contribute to the development of biomarkers that will help predict issues such as how the disease presents, response to treatments, development of future damage and other longer-term outcomes via linkage with routinely collected clinical data. Taken together with other emerging information, and collaboration in large consortia like HIPPOCRATES, results from this study will contribute to better diagnosis and use of therapies in patients with PsA, helping clinicians make better informed decisions in clinic and leading to better outcomes for patients with PsA.

In addition to the direct findings of SOPHOS, the data and samples form an important resource that is available to other researchers, via a dedicated access committee that reviews all applications, to study important questions in PsA and related immune rheumatic conditions. These results and data will support the precision medicine ecosystem in Scotland and internationally.

While not a direct aim of SOPHOS, the dedicated training relating to PsA assessments provided to clinical sites across Scotland as part of this study has helped improve clinical skills and PsA expertise at these sites, such that many of these assessments are now widely incorporated in routine NHS clinical practice across Scotland. In addition to direct clinical benefits for patients with PsA, this training and experience has also allowed several of these sites to contribute to subsequent academic and commercial interventional PsA studies, which would not have been possible without this training, thereby increasing research capacity in this domain across Scotland and giving more patients with PsA the opportunity to participate in clinical trials.

HOW WILL THE OUTCOMES BE DISSEMINATED?

SOPHOS has been presented at the Scottish Society for Rheumatology national conferences. Results of the study are being prepared for presentation at relevant international scientific and medical conferences and for publication in peer-reviewed scientific journals. In line with the permissions of the study, there will be ongoing analysis and collaboration using the data and samples for a range of clinically relevant questions and to support future funding applications. This data will also feed into political and public engagement groups such as the Scottish government arthritis cross-party group, NHS Scotland events, our local public engagement activities and international PPI events such as those run by GRAPPA.

CONCLUSION

PsA is a complex and heterogeneous disease with significant unmet clinical need. Patients with new or recent onset PsA have a significant clinical disease burden and impact. Studying the condition in its early stages will increase understanding of the condition, how it presents and develops and how patients are likely to respond to therapies. These will all contribute to improved outcomes for patients with PsA.

RESEARCH TEAM & CONTACT

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Additional Information

The study ended on 30th November 2023 and received £225k of funding from the Chief Scientist Office as well as funding from UCB Pharma