This project has received funding from the European Union’s Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 801604.
Low back pain is a common condition and one of the leading cause of life years lost to disability globally. The consequences of low back pain on the individual, healthcare systems, industry, and the wider society are considerable.

The recent NICE guidelines for low back pain identified exercise therapy as a central component of the treatment pathway. The guidelines fall short of recommending any one particular form of exercise, with best evidence suggesting that no one form of exercise is superior to another. Within clinical practice multiple forms of exercise therapy exist including but not limited too aerobic exercise, strengthening/muscular endurance exercise, motor control exercise, hydrotherapy, and stretching exercise.

It may be that exercise therapy, and indeed specific types of exercise, may be more beneficial for some patients compared to others. Ideally, using a precision medicine approach, those who would be most likely to benefit from exercise therapy (responders) could be identified and referred to this intervention. This logic could be extended in order to match the patient to the specific type of exercise most appropriate to them.

While such a precision medicine approach makes intuitive sense, it is based upon a logic which assumes that responders and non-responders to the exercise exist, i.e. that the response heterogeneity is clinically meaningful. Previously, authors within the pain literature have suggested that there is wide variability in response to treatment from the intervention arms of randomised controlled trials and proposed that this demonstrates that there are responders and non-responders to certain treatments. However, these studies are fundamentally flawed as they do not consider the natural random variability between the same baseline and follow-up time points that can be seen within the control group. As such they erroneously
assume inter-individual differences exist for a certain intervention and thus encourage research to investigate if specific exercises can be matched to certain patients to maximise outcome. This could lead to a considerable waste of research time and resources. In contrast if inter-individual differences in responses to certain interventions exist, this could help inform future research to explore the potential of precision medicine for that specific intervention in that specific population.

Our team have pioneered a new statistical approach for identifying if true inter-individual differences to interventions exist. This statistical technique has never been used to investigate if true variation in response to exercise occurs in people with low back pain. Such work would identify if matching patients to exercise therapy (and specific forms of exercise) is logical.

### Aim (400 words)

The aim of this PhD programme is to investigate if true and clinically important inter-individual differences in response to exercise therapy exist for people with low back pain.

The primary outcomes of interest will be pain and function. The secondary outcomes of interest will include a range of psychosocial outcome measures including measures such as pain related fear, mood, pain self-efficacy, catastrophizing, distress and quality of life.

### Methods

This PhD programme will include systematic review and secondary analysis of publicly available databases. These two methodological approaches will be combined with our novel true inter-individual differences analysis.

Systematic reviews of the literature investigating exercise therapy for people with low back pain will be undertaken. The review will look at exercise therapy as a single entity and then be further broken down into the main exercise therapy sub-types including but not limit to; aerobic exercise, strengthening.
exercise and motor control exercises. Appropriate inter-individual differences analysis will be undertaken to investigate if true variability in response to exercise (and different types of exercise) occurs or not.

Key, high quality, randomised controlled trials (such as the UK BEAM trial) that have investigated the effectiveness of exercise therapy for people with low back pain will be identified from the systematic review process. Then, where possible (i.e. the data are available on a publicly available database or can be obtained from the original authors), the true inter-individual differences approach will be applied at the individual patient level to further investigate if true variability in response to exercise (and different types of exercise) occurs or not.

| Strategic Relevance (300 words) | This work applies novel statistical methods to an important clinical question, applying the field of precision medicine to low back pain, a leading cause of disability worldwide. This cutting edge interdisciplinary work will open up an entirely new area of research within the field of pain management. The work will be undertaken within the strategic structures that exist within Teesside University – The Centre for Rehabilitation and Exercise Science (CRESS) and the Health and Wellbeing Grand Challenge. The latter structure aims to promote interdisciplinary work to create cutting edge research programmes while the former seeks to undertake research which will help patients to achieve their “personal best” within the context of their biological, psychological and social environment. This programme of work has the potential to catalyse a large programme of work in the area of inter-individual responses to a variety of interventions (i.e. pharmacology, surgery, manual therapy etc.) with potential for Teesside University to become world leading in this area by combining two independent areas in which it is already strong, specifically pain management and biostatistics. |
| Interdisciplinarity and fit with DTA3 | This is a truly interdisciplinary project bringing together researchers from the areas of physiotherapy, pain management, biostatistics and sports and exercise science. Professors Greg |
Atkinson and Alan Batterham are biostatisticians that have developed and refined a novel approach to quantifying the inter-individual variability of patient’s response to treatment contextualised against the normal response variability seen in control group participants. Professor Denis Martin and Dr Cormac Ryan are physiotherapists with a track record of investigating conservative interventions, including exercise, for people with low back pain. Dr Shaun Wellburn, is an early career researcher in the field of sports and exercise science with a special interest in the field of low back pain. This interdisciplinary team brings together expertise from these three different fields of study to create a highly novel PhD program. In addition, Professors Atkinson, Batterham, Martin and Dr Ryan all have experience of supervising DTA students.

The program of work fits with the Applied Biosciences for Health strand of the DTA. The primary outcome measures of interest in this work are pain and function for people with low back pain.

<table>
<thead>
<tr>
<th>Industrial Relevance (300 words)</th>
<th>There are no intended placements as part of this project. However, there may be opportunity to work with external partners who collaborate with supervisory team in this area of research.</th>
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<tr>
<td>Economic and Societal Impact (300 words)</td>
<td>Low back pain is one of the leading causes of disability worldwide. The economic consequences of low back pain are substantial. The cost of back pain to the UK economy is over 2.1billion annually. Exercise is a cornerstone of pain management in people with low back pain. Currently, there is no evidence that identifies which patients might benefit most from which types of exercise. Such a precision medicine approach could have considerable positive implications for patients and lead to efficiencies within the health service. A crucial first step to identifying if patients could be matched to specific exercises is to identify if true inter-individual variability in response to exercise therapy exists in people with low back pain.</td>
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#### Specific Admission Requirements

The candidate should have a 2:1 degree or better in a relevant discipline such as sports and exercise science, physiotherapy or statistics. A Master’s degree is preferable but not essential. Previous experience of systematic reviewing is desirable as is previous experience of undertaking quantitative statistical analysis.

| Minimum IELTS score | IELTS 6.5 with no lower than 6.5 in any element. |