Neuromuscular electrical stimulation to improve muscle weakness in hip osteoarthritis: A feasibility study

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Copywrite statement

Abstract

Title: Neuromuscular electrical stimulation to improve muscle weakness in hip osteoarthritis: A feasibility study

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Current rehabilitation practice in joint replacement surgery for the treatment of end-stage hip osteoarthritis may be ineffective at producing a level of neuromuscular activation required to induce a muscle strength adaption before and after surgery and therefore innovations are required. Neuromuscular electrical stimulation (NMES) is the elicitation of muscle contraction using electric impulses that can restore and increase skeletal muscle mass when voluntary exercise is limited due to pain during joint loading. The scoping review conducted in this integrated thesis identified i) a paucity of research exploring NMES interventions in individuals with hip osteoarthritis and ii) emerging evidence in related patient populations to support NMES for improving muscle strength and function. These findings shaped the design of a case-control study that compared lower limb strength in individuals with hip osteoarthritis to their healthy counterparts. When compared to a control group, weakness was observed in the maximal strength of the knee extensors (-22%), knee flexors (-34%) and hip abductors (-46%), but knee extensor endurance was the most considerably impaired measure in the affected (-70%) and contralateral limb (-62%) of those with hip osteoarthritis. An acceptability study followed and found that NMES of the knee extensors was tolerable and effective at producing an involuntary muscle contraction. However, it was difficult to stimulate the hip abductor muscles at an intensity acceptable to the participant due to pain and discomfort. A systematic review was later conducted to evaluate adherence levels to NMES interventions in orthopaedic populations and identify strategies to increase compliance. These strategies were combined with findings from the early experimental work to underpin a feasibility study that evaluated a six-week, home-based NMES intervention applied to improve knee extensor endurance in older adults. The intervention was successful at improving bilateral knee extensor endurance, maximal strength, mobility, and muscle size, and found high adherence to the intervention with favourable feedback from the NMES users. This study suggests that NMES of the knee extensors is a feasible and acceptable treatment modality for people with hip osteoarthritis that may lead to improvements in muscle endurance and mobility. Due to the non-weight bearing nature of NMES, this intervention could be applied before or after joint replacement surgery, and therefore these findings are important to inform current rehabilitation practice in hip osteoarthritis. Future research should involve assessing the intervention described here in a clinical setting, with a longitudinal design, to establish the long-term benefits of NMES on patient mobility.

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Integrated papers

In line with the alternative formats of thesis outlined within BU's Research Degree Code of Practice, this thesis follows and integrated format, where three published research articles, and one article in preparation for publication, are integrated into the thesis. Furthermore, sections of the literature review presented in Chapters 3 and the narrative review presented in Chapter 6 have been published. The table below provides the details of the included research articles, publication status, and location within this thesis. For co-authored publications, I am the lead author, and can confirm that I contributed over 75% of the substantive content of each article.

Paper	Reference	Chapter/section	Page numbers	Publication status
1	Burgess, L. C., Swain, I. D., Taylor, P. and Wainwright, T. W., 2019. Strengthening Quadriceps Muscles with Neuromuscular Electrical Stimulation Following Total Hip Replacement: a Review. Cur Phys Med Rehabil Rep, 7, 275-283	Chapter 3 Section 3.4.1	41-43	Published
2	Burgess, L. C., Taylor, P., Wainwright, T. W. and Swain, I. D., 2021. Strength and endurance deficits in adults with moderate-to-severe hip osteoarthritis, compared to healthy, older adults. Disabil Rehabil, 44 (19) 5563-5570.	Chapter 4 Section 4.4	53-61	Published
3	Burgess, L. C., Taylor, P., Wainwright, T. W. and Swain, I. D., 2021. Lab-based feasibility and acceptability of neuromuscular electrical stimulation in hip osteoarthritis rehabilitation. J Rehabil Assist Technol Eng, 16 (8).	Chapter 5 Section 5.4	68-79	Published
4	Burgess, L. C., Venugopalan, L., Badger, J., Street, T., Alon, G., Jarvis, J. C., Wainwright, T. W., Everington, T., Taylor, P. and Swain, I. D., 2021. Effect of neuromuscular electrical stimulation on the recovery of people with COVID-19 admitted to the intensive care unit: A narrative review. J Rehabil Med, 53 (3).	Chapter 6 Section 6.4.3	85-87	Published
5	Burgess, L. C., Taylor, P., Wainwright, T. W., Bahadori, S. and Swain, I. D., 2021. Adherence to Neuromuscular Electrical Stimulation Interventions for Muscle Impairment in Hip and Knee Osteoarthritis: A Systematic Review. Clin Med Insights Arthritis Musculoskelet Disord, 14.	Chapter 7 Section 7.4	91-106	Published
6	Burgess, L. C., Taylor, P., and Swain, I. D., Six-weeks of home-based NMES improves knee extensor endurance and function in healthy, older adults – A feasibility study.	Chapter 8 Sections 8.2 – 8.6	109-132	In preparation

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Chapter 1. Introduction

1.1 Chapter introduction

The aim of this study is to explore the feasibility of neuromuscular electrical stimulation (NMES) to counteract muscle weakness in individuals with hip osteoarthritis, who may require treatment with joint replacement surgery. This contribution to the evidence-base is important on both a local and national scale, as the older population in the United Kingdom (UK) and worldwide continues to increase. With increased age comes an increased risk of orthopaedic diseases, the most common of which is osteoarthritis. Furthermore, rehabilitation challenges exist for individuals with hip osteoarthritis undergoing hip replacement surgery, and therefore innovations in current practice are required. This chapter provides an overview of the rationale for this research, the research objectives and thesis outline.

1.2 Background

Total hip replacement surgery has for some time been recognised as a clinically successful and cost-effective surgical procedure for the treatment of hip osteoarthritis (Learmonth et al. 2007). However, while improvements in patient mobility and physical functioning following this procedure are well-documented, many patients experience ongoing functional deficits, and do not return to their pre-surgery level of physical activity (Smith et al. 2017; Smith et al. 2018). Furthermore, preliminary work has found that the current standard care for rehabilitation following hip replacement surgery is ineffective at producing a level of neuromuscular activation required to induce a muscle strength adaption (Gavin et al. 2018) and has no effect on patient function or quality of life in the six weeks or twelve months following surgery (Smith et al. 2008; Smith et al. 2009), as discussed further in Chapter 2. Therefore, there is a need to develop alternative and innovative treatment regimens that can be used to enhance longer-term recovery and are feasible for people with end-stage hip osteoarthritis pre and postoperatively. NMES is a treatment that can facilitate exercise and counteract muscle impairment in adults with advanced progressive diseases undergoing surgery, who have difficulty activating their muscles voluntarily, yet research in this area remains limited (Spector et al. 2016; Nussbaum et al. 2017). It has been proven to enhance muscle strength, increase range of motion, reduce oedema, prevent atrophy, heal tissue, and decrease pain in a variety of patient and athlete populations, as discussed further in Chapter 3; however, more research is required in NMES and individuals with hip osteoarthritis.

1.3 Rationale

New technologies have the potential to revolutionise how we manage health conditions, and recovery from major surgery, both now and in the future. The rationale for undertaking this study evolved from a collaboration between the Orthopaedic Research Institute (ORI) of Bournemouth University, and

Odstock Medical Ltd. Odstock Medical was established by the Salisbury NHS Foundation Trust, to build expertise on electrical stimulation devices. ORI works across Bournemouth University and with hospitals, industry partners and academia to produce research that can improve outcomes of patients with hip osteoarthritis. ORI worked closely with Odstock Medical to develop an Orthopaedic NMES device (Figure 1), created for general orthopaedic use and for following joint replacement surgery. The device has already passed external safety testing, and is CE marked, and therefore was not under investigation. Rather, this project sought to understand the potential benefits of using the device for patients with hip osteoarthritis, who may require treatment with hip replacement surgery.

Figure 1. Odstock Medical Ltd orthopaedic stimulator

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1.4 An introduction to neuromuscular electrical stimulation

Neuromuscular electrical stimulation (NMES) is, in its simplest definition, the elicitation of muscle contraction using electric impulses. It involves the application of electrical impulses to the nerves that supply skeletal muscles, by means of surface electrodes placed over the muscle belly, with the goal of evoking involuntary muscular contractions (Spector et al. 2016) (Figure 2). NMES is an alternative treatment to voluntary exercise that can provide physiologic gains without increasing mechanical load and has proven effective in facilitating exercise and counteracting muscle impairment in adults with advanced progressive diseases (Jones et al. 2016). Importantly, it offers unique advantages to preserve or restore skeletal muscle mass and function before, during and after a period of disuse due to injury, surgery, or illness, where voluntary exercise is difficult or not possible (Kramer and Mendryk 1982; Jones et al. 2016). It can be used as an adjunct modality to enhance the strengthening effects of an

existing rehabilitation programme, or support patients with muscle weakness who cannot tolerate high-intensity exercise or a high-volume of low-intensity exercise (Jones et al. 2016).

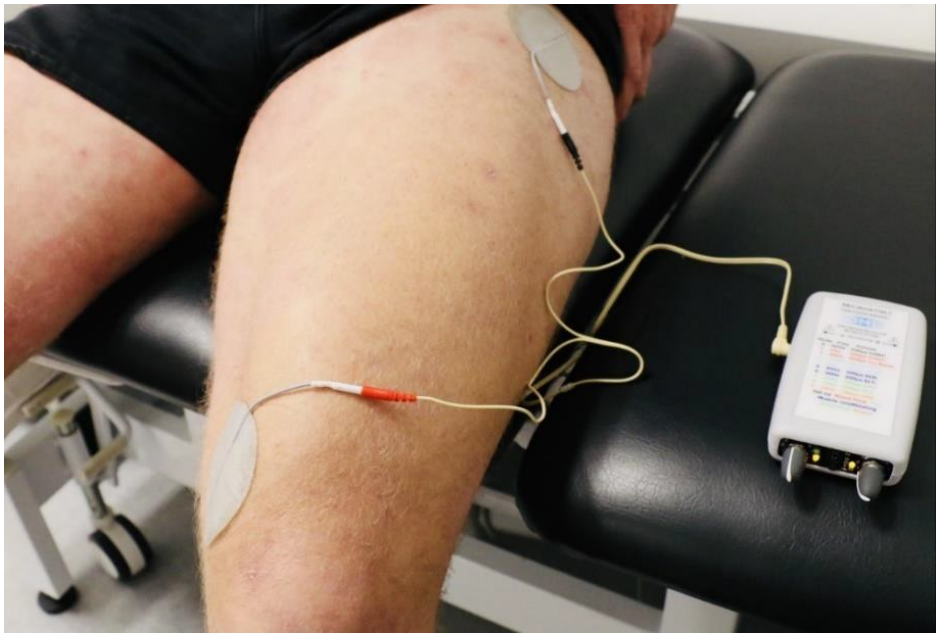


Figure 2 NMES applied to the quadricep muscles

Own image

Although it is largely acknowledged that the force contracted through electrical stimulation is not greater than voluntary, isometric contractions, it can be used to preserve or restore skeletal muscle mass and function following periods of muscle atrophy due to immobilisation (i.e. bed rest following surgery) (Dirks et al. 2014). Electrical stimulation can also be applied preoperatively, where pain prevents voluntary exercise and in the early phase of rehabilitation following surgery when voluntary contractions are not feasible due to pain, swelling or immobilisation, but muscle atrophy is prominent (Kouw et al. 2019). Electrical stimulation can produce a muscle contraction without the requirement of mobilisation or joint loading, and therefore may be advantageous in these circumstances. Following the immediate postoperative phase, electrical stimulation combined with exercise interventions has been advocated as an optimal treatment strategy, as the adaptions evoked by electrical stimulation are not just confined to the activated muscle but also involve neural adaptions through reflex inputs to the spinal cord and supraspinal centres (Vanderthommen and Duchateau 2007). However, despite the supporting evidence, NMES remains a clinically underutilised treatment modality in the orthopaedic population (Peter et al. 2014; Spector et al. 2016), and is not currently recommended by NICE in osteoarthritis due to the limited and heterogenous evidence to support its use (NICE 2022). Reasons for limited adoption reported in the literature include a lack of guidelines on stimulation interventions and parameters, uncertainty regarding the efficacy of stimulation for strengthening muscles and concerns of pain in patients particularly sensitive to electrical stimulation

(Spector et al. 2016). Further investigation of electrical stimulation devices has been warranted, with particular focus to their use immediately post-surgery and in accelerating the recovery of muscle function during post-discharge rehabilitation (Bandholm et al. 2018).

1.5 Aims and objectives

The broad aim of this study was to examine the feasibility of NMES for improving muscle weakness in adults with hip osteoarthritis who may require treatment with hip replacement surgery. The objectives of this study are described in Table 1.

Objective	Methodology	Chapter(s)
1. To gain an understanding of the physiological deficits and rehabilitation challenges common in individuals with hip osteoarthritis.	Literature review Quantitative, lab-based study	Chapter 2 Chapter 4
2. To learn whether NMES is an acceptable and tolerable treatment modality for individuals with hip osteoarthritis.	Literature review Mixed-method lab-based study. Systematic review on adherence.	Chapter 3 Chapter 5 Chapter 7
3. To assess the feasibility of using NMES to improve the physiological deficits and rehabilitation of individuals with hip osteoarthritis who may require treatment with hip replacement surgery	Feasibility study	Chapter 8

Table 1 Study objectives

1.6 Methodological overview

To integrate novel medical devices into clinical practice, quantitative approaches are needed to create scientific objectivity and justification for their use (Carr 1994; McCusker and Gunaydin 2015). Therefore, this study primarily used quantitative research methods to collect, analyse and interpret data on NMES use in the target population. The study used a combination of descriptive, observational, and experimental research to draw conclusions regarding the research objectives described above. In addition, as this research sought to understand user perspectives of NMES, it also collected some qualitative data, whereby participants were able to give their feedback on their acceptability and the usability of the device. Given the integrated format of this thesis, the full methodology for each research study is described within its respective chapter.

1.7 Thesis outline

This integrated thesis is divided into ten chapters, including three published research papers, and one research study in preparation for journal submission. In addition, sections of the literature review presented in Chapters 3 and the narrative review described in Chapter 6 have been published. Chapter 2 provides an overview of the current practice and evidence in hip osteoarthritis and hip replacement surgery, and where challenges remain. Chapter 3 introduces NMES, including important definitions and physiological considerations when prescribing it. In addition, Chapter 3 includes sections of a scoping review that summarises the available evidence for NMES applied for strengthening purposes in lower limb orthopaedic populations. Chapter 4 is a published case-control study, examining physiological deficits in adults with hip osteoarthritis in comparison to their healthy counterparts, including a comparison of maximal isometric strength and isotonic endurance, to inform the design of the study described in Chapter 8. Similarly, Chapter 5 evaluates the feasibility and acceptability of NMES applied to the knee extensors and hip abductor muscle groups in the hip osteoarthritis population through measures such as pain, discomfort, and muscle contractile force. Chapter 6 briefly describes the Covid-19 pandemic, and how it affected the methodology of this research. Chapter 7 is a published systematic review, summarising adherence rates to NMES interventions for muscle impairment in hip and knee osteoarthritis, and strategies to increase adherence. Chapter 8 is a feasibility study, assessing the effectiveness of a six-week, home-based NMES intervention for increasing knee extensor muscle endurance in a healthy, older adult population. Chapter 9 discusses the research conducted, it's collective strengths and limitations, and provides recommendations for future research and practice. Finally, Chapter 10 concludes the research in relation to the thesis aim.

1.8 Chapter summary

Hip osteoarthritis is increasingly prevalent within an aging population, and while outcomes from hip replacement procedures continue to improve, significant functional deficits remain for some. Current rehabilitation practice has been considered ineffective at facilitating a return to activities of daily living, and therefore innovations are needed to improve clinical care. NMES is an innovative treatment modality that may help to strengthen weakened musculature, increase muscle endurance, prevent atrophy, and improve functional ability in individuals with hip osteoarthritis, who may require treatment with hip replacement surgery. Nonetheless, application of NMES devices in this population has so far been slow, and questions remain regarding the feasibility of applying NMES to individuals with hip osteoarthritis. Therefore, this thesis aimed to investigate the feasibility of NMES to improve muscle weakness in this patient population and provide recommendations for future research.

Chapter 2. Current evidence and practice in hip osteoarthritis

2.1 Chapter introduction

To underpin the research undertaken in this thesis, the following chapter provides an overview of hip osteoarthritis, indications for surgery, and the development of hip replacement surgery over time. It includes a synthesis of muscle weakness in osteoarthritis, and how this is related to longer-term recovery from surgery. The chapter continues by discussing current physiotherapy practice in hip osteoarthritis, and the rehabilitation challenges yet to be resolved. The potential role of NMES to overcome the existing rehabilitation challenges is introduced and expanded on in Chapter 3.

2.2 An overview of hip osteoarthritis

2.2.1 Definition

The National Institute for Health and Care Excellence (NICE) defines osteoarthritis as a disorder of the synovial joints, which occurs when damage triggers repair processes that lead to structural changes within a joint (NICE 2022). Joint damage may occur through repeated excessive loading and stress of a joint over time, or by injury. Osteoarthritis results from a combination of the breakdown of the joint and the body's attempted repair processes. These repair processes may alter the structure of the joint, causing a loss of localised cartilage, remodelling of adjacent bone and the formation of osteophytes, and inflammation of the synovial membrane (NICE 2022). In a qualitative study of the patient experience of hip osteoarthritis, the time from the onset of osteoarthritis to the preoperative stage of a hip replacement was described as "life restricted by pain and disability" (Fujita et al. 2006).

2.2.2 Indications

A diagnosis of osteoarthritis may be considered if the patient is aged 45 years or older and has a history of activity-related joint pain, functional impairment and has no morning joint stiffness, or stiffness that lasts no longer than thirty minutes (NICE 2022). Upon clinical examination, symptoms of osteoarthritis may include: i) joint swelling ii) joint instability and deformity; iii) joint warmth or tenderness; iv) muscle wasting and weakness and v) restricted and painful range of movement (NICE 2022). In patient-focused studies, those with osteoarthritis report pain, functional limitations, reduced quality of life and impaired work productivity and activity (Jackson et al. 2020). In a study examining pain drawings by those with hip osteoarthritis, the most common locations of pain presented in the greater trochanter, groin, thigh, and buttock areas (Poulsen et al. 2016).

2.2.3 Incidence and treatment

In the United Kingdom (UK), around a third of women and a quarter of men aged between 45 and 64 have sought treatment for osteoarthritis, and this number rises to almost half of people aged over 75 years (Versus Arthritis 2019). 2.46 million (10.9%) adults aged over 45 have osteoarthritis of the hip,

the primary indication for hip replacement surgery (91.3%) (National Joint Registry 2021). Other indications for hip replacement include hip fracture, avascular necrosis, congenital dislocation and inflammatory arthroplasty (National Joint Registry 2021). Prior to treatment with joint replacement surgery, guidelines from NICE recommend that patients receive education, advice and access to information of self-managing their condition, combined with therapeutic exercise (local muscle strengthening and aerobic fitness training) and weight loss if necessary (NICE 2022). Furthermore, NICE guidelines recommend that clinicians consider prescribing oral analgesics, topical treatments, non-steroidal anti-inflammatory drugs, and intra-articular injections to help manage pain.

When non-surgical efforts to manage pain and stiffness become ineffective, and symptoms begin to affect the patient's quality of life, NICE guidelines recommend consideration of hip replacement surgery to treat end-stage hip osteoarthritis (NICE 2022). Since data was first collected by the National Joint Registry in 2003, the total number of hip replacements recorded is 1,251,164 (National Joint Registry 2021). More women (59.9%) have undergone surgery than men (40.1%), and the mean age at implantation across all patients is 68 years (National Joint Registry 2021).

2.3 The development of total hip replacement surgery

Total hip replacement, also termed total hip arthroplasty, is a surgical procedure that replaces the hip joint with an artificial prosthesis (Siopack and Jergesen 1995). The hip joint is replaced by a prosthetic ball and socket, that replicates the shape and movement of the natural joint (Figure 3). This procedure differs from a partial hip replacement, where only the ball (head of the femur) is replaced, which is more commonly used in cases of hip fracture, rather than arthritis. Total hip replacement surgery has for some time been acknowledged as both clinically and cost effective for patients and health care providers (Chang et al. 1996; Learmonth et al. 2007).

Figure 3 Total hip replacement surgery

Used with permission of the Orthopaedic Research Institute, Bournemouth University

Total hip replacement has seen significant change over time, with the first prosthetic hip developed in 1938 (Wiles 1958). Early endeavours were largely limited by poor designs, inferior materials and mechanical failure (Learmonth et al. 2007). In 1961, John Charnley documented a new method, described as low friction arthroplasty (Charnley 1961). Charnley also introduced the use of acrylic cement to fix components to bone and high-density polyethylene as a bearing material (Charnley 1961). Metal on polyethylene articulations began to dominate by the 1970s, with the Exeter hip becoming a highly influential and commonly used prosthesis (Fowler et al. 1988). The 1990s saw the growth of the metal-on-metal articulation with the Birmingham Hip Resurfacing (Daniel et al. 2014) preserving the femoral head by screwing a metal cap onto the head. However, following high failure and revision rates of the large head metal-on-metal articulation, and potential exposure risk to dangerous metals such as chromium and cobalt, the number of metal-on-metal articulations reduced and are now rarely used (Clarke et al. 2015). Today, metal-on-polythene is the most commonly used bearing construct across cemented, uncemented and hybrid hip replacements, although the use of ceramic-on-polyethylene bearings continues to grow (National Joint Registry 2021). The most common indications for revision hip replacement surgery remain aseptic loosening, dislocation (instability), adverse reaction to particulate debris, pain, infection and periprosthetic fracture (National Joint Registry 2021).

2.3.1 Enhanced Recovery after Surgery

Over the last fifteen years, the systematic implementation of an evidence-based perioperative care protocol (named “fast-track” or “enhanced recovery pathway”), has shown that hospital length of stay and complications can be reduced for a number of surgical procedures (Ljungqvist et al. 2017). This includes hip replacement surgery, where high-volume models have demonstrated a reduction in length of stay from 4-10 days to 1-3 days, and outpatient surgery is possible for around 15% of patients in unselected cohorts (den Hartog et al. 2013; Kehlet 2013; Khan et al. 2014; Aasvang et al. 2015; Gromov et al. 2017). The patient-centred approach to hip replacement surgery aims to minimise the surgical stress response and accelerate the achievement of discharge criteria (Soffin and YaDeau 2016). Enhanced recovery pathways are now frequently delivered as standard practice for hip replacement surgeries, and surgical protocols include preoperative patient education, adopting local anesthetic techniques in combination with an opioid-sparing multimodal analgesic approach and early mobilisation following surgery (Wainwright et al. 2020b).

2.3.2 Minimally invasive surgery

Minimally invasive total hip replacement has been developed, whereby a smaller cut (around 10 cm) is made to the skin, as opposed to conventional hip replacement, where the cut would be between 20 and 30 cm. There is evidence that supports minimally invasive surgery for reducing operative time

and blood loss following hip replacement (Cheng et al. 2009). Other benefits are reduced soft-tissue damage, postoperative pain, and accelerated discharge and recovery (Learmonth et al. 2007).

2.3.3 Computer-assisted total hip replacement

A recent development of total hip replacement is computer-assisted surgery, whereby robotics can increase the accuracy of implant placement (Subramanian et al. 2019). Accurate positioning of implants is key to achieve a good clinical outcome, and computer assisted navigation can improve the precision of the acetabular cup placement by decreasing the number of outliers from the desired alignment (Gandhi et al. 2009). Despite the substantial advancements in this area, computer assisted total hip replacement use is limited due to the steep learning curve, technical issues, such as robot failure, and high cost. However as technology and evidence for improved outcomes continues to evolve, a greater adoption of computer-assisted total hip replacement is anticipated (Chang et al. 2017).

2.3.4 The future of hip replacement surgeries

The rising global life expectancy, an increasing prevalence of obesity and extending the surgical indications to younger adults have contributed to a gradual rise in the volume of hip replacement surgeries occurring annually (Maloney 2001; Kurtz et al. 2005; Culliford et al. 2010), as demonstrated in Figure 4 using data from the National Joint Registry. Projections based upon demographic trends suggest that hip replacement surgeries will continue to increase at growth rate of 134% between 2012 and 2030 in England and Wales (Patel et al. 2015). These predictions are similar to forecasts from the United States, which estimate primary hip replacement surgeries to grow by 174% between 2005 and 2030 (Kurtz et al. 2007). With a hip replacement costing the NHS around £7000, treatment of end-stage hip osteoarthritis presents a significant economic burden. Improving outcomes from hip replacement surgery, and reducing the rehabilitation burden, may offer considerable benefits to patients and healthcare systems.

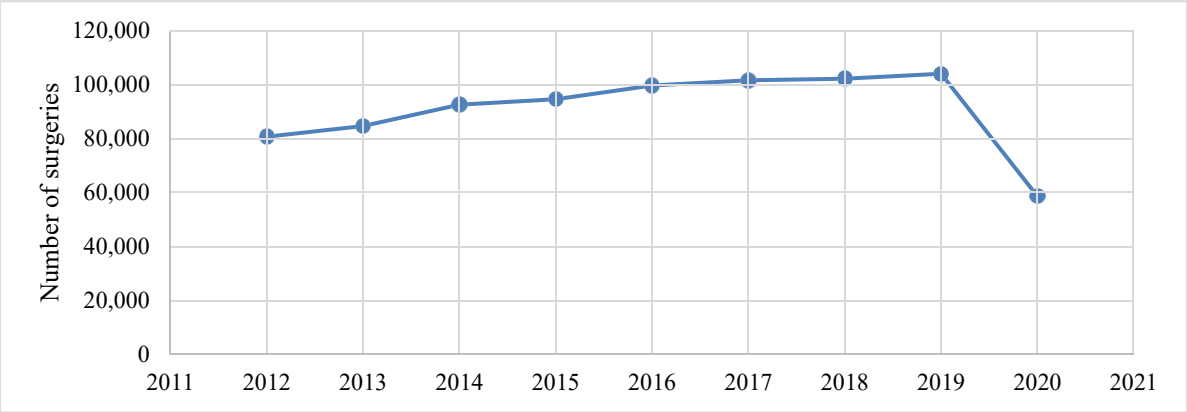


Figure 4 Primary hip replacement procedures in England, Wales, and Northern Ireland, registered on the National Joint Registry, per year*
(National Joint Registry (NJR) 2022)

**Data only available until 2020. Surgery volume from 2020 affected by the Covid-19 pandemic.*

2.4 Outcomes from hip replacement surgery

The technical development of prostheses, advances in surgical techniques and development of enhanced recovery pathways described above have led to increasingly successful clinical outcomes for patients having their hip replaced (Ethgen et al. 2004; Beswick et al. 2012; Bengtsson et al. 2017). Enhanced recovery protocols have been proven as successful for minimising the surgical stress response and accelerating the achievement of discharge criteria (Morrell et al. 2021). As a result, length of stay continues to decrease, with no increase to perioperative morbidity or readmission (Morrell et al. 2021). Data from the Arthritis Foundation highlights that 90% of patients who had moderate pain pre-surgery, and 89% of patients with severe pain, report mild or no pain five years following surgery (Arthritis Foundation 2022). In addition, according to patient reported outcome measures (PROMs), such as the Oxford Hip Score and the Harris Hip Score, total hip replacement surgery is successful in improving self-reported function (van der Wees et al. 2017). However, discrepancies have been found when comparing the results of PROMs to performance-based function measures (Luna et al. 2017). While improvements in patient mobility and physical functioning following lower extremity joint replacement surgery are documented for some, significant postoperative functional deficits remain in others, whereby patients struggle to return to activities such as walking, climbing stairs, and getting in and out of a car five years after surgery (Beswick et al. 2012; Astephen Wilson et al. 2019; Arthritis Foundation 2022).

Functional recovery is an important target of recovery (Aahlin et al. 2014), and the ability to regain mobility and strength is vital to enable a patient to complete activities of daily living independently. In a study of 411 primary total hip and knee replacements, patient satisfaction was reported at 89% for hip replacement surgery and the most common reasons for dissatisfaction were persistent pain (41%),

functional limitation (35%) and slow recovery (6%) (Halawi et al. 2019). Furthermore, research suggests that that physical activity levels often do not increase after surgery (Withers et al. 2017), and in some cases, patients are less active at two year follow-up than before hospital admission (Smith et al. 2017; Smith et al. 2018). These findings raise much concern; given that a motivation to undergo joint replacement is often to improve function. In addition, these findings must be addressed due to the association between physical inactivity and the development of numerous non-communicable diseases, such as coronary heart disease, type 2 diabetes, and cancer (Lee et al. 2012).

Given the success of enhanced recovery surgical pathways in hip replacement, researchers are now focusing on post-discharge recovery, and how physical rehabilitation can be used to help patients return to optimal function (Bandholm et al. 2018). Joint replacement surgery will continue to be used as a treatment option for those with end-stage osteoarthritis. Therefore, while it is important to continually improve the surgical procedure itself, perioperative rehabilitation strategies also require research attention (Astephen Wilson et al. 2019). It is thought that strengthening patients in the pre and postoperative phase may lead to better functional outcomes in the longer-term, however the evidence base is varied. The following sections of this chapter will discuss muscle weakness in hip osteoarthritis, and the evidence for current rehabilitation strategies.

2.5 Muscle weakness in hip osteoarthritis

Sarcopenia is a condition characterised by a loss of skeletal muscle mass and function and remains a clinical problem that impacts millions of older adults (Santilli et al. 2014). People with conditions such as rheumatoid arthritis and osteoarthritis may be at an increased risk of sarcopenia, which is correlated with poor function and quality of life (Santilli et al. 2014; Kemmler et al. 2015). While resistance training can overcome sarcopenia, older adults may be reluctant to perform voluntary exercise, particularly those with chronic pain or poor mobility. Studies have shown that less than 15% older adults regularly participate in resistance training (Merom et al. 2012), with barriers to participation including poor health, fear of risk of injury or pain, fatigue, low self-efficacy, lack of time, knowledge or resources and a fear of risk of heart attack, stroke or death (Burton et al. 2017). Participation may be even lower in older adults with osteoarthritis, due to severe pain and biomechanical changes to the joint that can alter their response to voluntary exercise (Latham and Liu 2010). This creates a significant rehabilitation challenge in the osteoarthritis population, particularly in those patients who require treatment with surgical intervention, yet present with persistent muscle atrophy and weakness.

Muscle weakness may occur in individuals with hip osteoarthritis for several reasons; factors associated with the pre-existing arthritis, but also factors related to obesity, morbidities, or age-related declines in muscle mass. Weakness may be caused by muscular changes (for example, atrophy or a decrease in the number and size of muscle fibres) or related to neuronal causes (such as reduced voluntary muscle activation). To date, the most thorough review of muscle weakness in hip

osteoarthritis has been conducted by Loureiro and colleagues in 2013. The review included thirteen studies evaluating muscle strength, muscle size, muscle quality and muscle inhibition in adults with hip osteoarthritis (Loureiro et al. 2013). The studies included in the review agreed that muscle strength, size and quality were reduced in the affected limb, when compared to the contralateral limb, in people with hip osteoarthritis. The greatest reductions in strength were observed in the hip and knee flexors and extensors, with less consistent evidence supporting the loss of muscle strength in the hip abductors and adductors. Just two studies compared muscle strength between individuals with hip osteoarthritis and a healthy cohort, with both reporting large effect sizes for lower hip abductor strength in the osteoarthritis group (Arokoski et al. 2002; Klausmeier et al. 2010). In the included studies, decreased muscle size (atrophy) in the affected limb when compared to the contralateral limb was consistently reported as the underlying mechanism for muscle weakness. In addition, assessments of muscle size found consistently strong evidence for reduced quadriceps size in affected the limb when compared to the contralateral limb, however moderate evidence was found for no difference in hip abductor size between legs. Likewise, in the studies comparing the individuals with hip osteoarthritis to a healthy cohort no difference was found in muscle size between groups, however it is possible these findings were confounded by the increase in body weight in the osteoarthritis group (Loureiro et al. 2013). Therefore, additional work is required to understand the true effect of hip osteoarthritis on muscle strength, as explored further in Chapter 4.

The force generated by a muscle is largely a result of the muscle's cross-sectional area and the level of motor unit activation (Bruce et al. 1997). Therefore, muscle weakness can result from either or both mechanisms. The amount of force that can be produced is directly proportional to the muscle's cross-sectional area. However, muscle quality will also affect strength, as the total cross-sectional area of a muscle is a measure of both contractile and non-contractile tissue, and in muscle atrophy, fatty tissue may occupy the space left by degenerating muscle fibres (Rahemi et al. 2015). In addition, the ability of the nervous system to fully activate a muscle plays a major role in determining the force production capacity of the muscle. Arthrogenic muscle inhibition describes the inability to fully activate a muscle secondary to joint dysfunction, such as osteoarthritis (Rice and McNair 2010). Failure to fully activate a muscle indicates an inability to recruit all motor units and/or a reduction in firing rate, and can occur due to factors such as swelling, inflammation, joint laxity and damage to joint afferents (Rice and McNair 2010).

The strength of muscles surrounding the hip play an important role in stabilising the joint, absorbing shock and protecting the joint from harmful and painful movements (Kak et al. 2016). For example, the hip flexors and extensors work together to maintain a neutral pelvis position and allow a powerful and safe range of motion through the hip (Neumann 2010). The hip abductor muscles contribute substantially to pelvic stabilisation during walking and running, and are primarily responsible for

generating moments of force to control frontal plane movement (Greco and Vilella 2022). In addition, the strength of knee flexor and extensor muscles is associated with the ability to perform functional tasks, such as rising from a chair, walking, and climbing stairs, and muscle weakness in these muscle groups has been associated with slower gait speeds, and an increased risk of falls (Ploutz-Snyder et al. 2002). Therefore, muscle weakness in hip osteoarthritis has important clinical implications due to its effect on symptom exacerbation and the ability to perform activities of daily living. In addition, muscle weakness before and after joint replacement surgery has been associated with a prolonged postoperative recovery (Buirs et al. 2016). For example, post-surgical gait function one year after surgery is correlated with pre-surgical gait function, which can be influenced by muscle atrophy and weakness (Foucher et al. 2007). Therefore, early intervention is required to strengthen lower extremity muscles in this patient population both pre and postoperatively (Loureiro et al. 2013).

2.6 Current practice in rehabilitation

An optimal exercise protocol to strengthen weakened musculature in individuals with hip osteoarthritis pre- or post-surgery has not been agreed on in the literature, and clinical guidelines are varied. For example, NICE do not recommend preoperative rehabilitation for all patients undergoing hip replacement, the Royal Dutch Society for Physical Therapy (KNGF) recommend it for those at risk of delayed recovery, and the American Academy of Orthopaedic Surgeons (AAOS) recommend it for all, albeit with limited overall strength of evidence (NICE 2020; van Doormaal et al. 2020; AAOS 2021). Postoperatively, guidelines from NICE (2020) for people who have had hip or knee replacement recommend that:

1. A member of the physiotherapy or occupational therapy team should give advice on self-directed rehabilitation.
2. This advice should be given before the person leaves hospital and adjusted to individual needs.
3. Supervised or individual outpatient rehabilitation should be offered to those who have:
    - Difficulties managing activities of daily living
    - Ongoing functional impairment
    - Find that self-direction rehabilitation is not meeting their rehabilitation goals
    - Have cognitive impairment.

Guidelines from America and the Netherlands are similar, whereby AAOS and KNGF recommend exercise therapy, with low to moderate certainty (van Doormaal et al. 2020; AAOS 2021). These recommendations are underpinned by the available evidence, however while evidence exists to support pre and post-operative exercise, it is often too varied and inconsistent to confirm an optimal rehabilitation regime through consensus agreement. In addition, measures of outcome related to the success of rehabilitation, such as length of stay in hospital, complications or PROMs do not always

correlate to improvement in performance based function or participation in physical activity (Aasvang et al. 2015; Luna et al. 2017).

2.6.1 Preoperative strengthening exercise

Preoperative exercise (prehabilitation) has gained much research attention over the last ten years. The concept of prehabilitation involves preparing a patient for surgery by improving their physical function in the preoperative phase. Prior to surgery, many patients avoid voluntary exercise due to fear of exacerbating pain or causing joint damage (Hunter and Eckstein 2009; Petursdottir et al. 2010; Dobson et al. 2016; Kanavaki et al. 2017; Hurley et al. 2018) and these preoperative changes in identity and lifestyle are reported to preclude a 'return to normal' following joint replacement (Terracciano et al. 2013). While some studies suggest a well-designed prehabilitation programme can improve pain, range of motion, physical function and postoperative outcomes, other studies report minimal or no benefit to the patient when compared to standard care or no exercise. These studies are described in further detail in this section.

Current evidence

Over the last ten years, numerous systematic reviews and meta-analyses have been conducted to compare outcomes for patients receiving preoperative exercise and those receiving standard care, however the level of evidence has remained low. In 2011, Wallis and Taylor found low to moderate quality evidence from nine studies that patients who completed exercise and education programmes before hip replacement surgery may have improved function and activity in the short term after surgery (Wallis and Taylor 2011). Similarly, Hoogeboom et al. included five studies of patients undergoing hip replacement in their systematic review and meta-analysis conducted in 2012 and concluded that preoperative therapeutic exercise in joint replacement surgery does not demonstrate beneficial effects on postoperative functional recovery (Hoogeboom et al. 2012). In 2013, Gill and McBurney found a medium treatment effect of preoperative exercise on pain and self-reported function when compared to a control group, but no treatment effect for strength or walk speed outcome measures when the individual studies were pooled (Gill and McBurney 2013).

Wang et al. (2016) later investigated prehabilitation in hip and knee replacement surgery and through a comprehensive systematic search, without limitations applied to the article language, date or publication status, found an additional seven randomised controlled trials (RCTs) that were not included in any previous published reviews (Wang et al. 2016b). Nonetheless, the authors found that the effects of exercise before joint replacement surgery on pain and function were still too small to be considered clinically consistent. Prehabilitation was found to slightly reduce pain scores within four weeks post-surgery however this difference did not persist beyond four weeks (Wang et al. 2016b). Likewise, WOMAC function scores, time to climbing stairs, toilet use, and chair use were slightly

improved at 6-8 and 12 weeks postoperatively. However, prehabilitation did not lead to a clinically important difference in quality-of-life scores, length of stay or total patient costs (Wang et al. 2016b). In the last two years, more systematic reviews in prehabilitation for lower limb joint replacement have emerged (Almeida et al. 2020; Vasta et al. 2020; Widmer et al. 2022), yet no further advances have been made. It remains that there is some evidence to support the effectiveness of prehabilitation in improving outcomes related pre and postoperatively, yet this is not conclusive, and further work is required. The authors call for innovative interventions that are effective in improving muscle strength and function, and that can be well tolerated by older adults awaiting joint replacement, and highlight the potential benefits of NMES and blood-flow restriction (Almeida et al. 2020).

2.6.2 Postoperative strengthening exercise

Following hip replacement surgery, muscle atrophy may occur due to immobilisation because of pain or long durations of bed rest. A recent study found that six days of hospitalisation following elective total hip replacement led to substantial leg muscle atrophy in patients aged over 75 years (Kouw et al. 2019). The authors of this study found a decline in quadriceps (-3.4% ± 1.0%) and thigh muscle (-4.2% ± 1.1%) cross-sectional area of the non-operated leg ($p<0.05$), and oedema resulted in a 10.3% ± 1.7% increase in leg cross-sectional area of the operated leg ($p<0.05$). However, while it seems that postoperative, exercise-based rehabilitation is superior to no rehabilitation after hip replacement surgery, there remains a need to identify the best dose of exercise and mode of delivery (Bandholm et al. 2018).

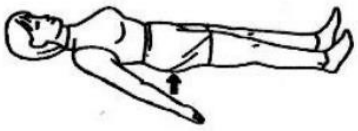
Current evidence

Following joint replacement surgery, early mobilisation, also termed early ambulation, is well established for reducing thromboembolic complications (Barker and Marval 2011; Jorgensen et al. 2013), respiratory complications (Boden et al. 2018), length of stay (Ibrahim et al. 2013; Mak et al. 2014), and the need for blood transfusion (Husted et al. 2008) without increasing the risk of complication or adverse events (Guerra et al. 2015). Early mobilisation involves encouraging patients to sit, stand and ambulate as soon as is safe postoperatively, and now supersedes bed rest as standard care following orthopaedic surgery, which has been associated with greater risk of thromboembolism, pneumonia, muscle wasting and physical deconditioning. It is a cornerstone of enhanced recovery pathways (Wainwright et al. 2019) and it is seen as best practice following many surgical procedures.

Once a patient is ready to return home, they will likely be discharged home with exercise advice in the form of a patient information leaflet and told to progress independently until their six week follow up (NICE 2020). Patient information leaflets often contain advice on recovery from surgery and exercise prescription in the form of bed exercises and sitting and standing exercises (Figure 5). While they can be beneficial to guide the patient through their postoperative recovery, preliminary work

found that information leaflets are often designed on a ‘one size fits all’ basis, and rarely offer advice on progressing the frequency or intensity of the exercise (Wainwright and Burgess 2018). In addition, earlier work has found that bed exercises are ineffective at producing a level of neuromuscular activation required to induce a muscle strength adaption (Gavin et al. 2018) and have no effect on patient function or quality of life in the six weeks or twelve months following surgery (Smith et al. 2008; Smith et al. 2009). Research has concluded that the time taken by physiotherapists teaching bed exercises may be more usefully spent on other treatments to optimise outcome, such as alternative exercise programmes or a greater intensity of gait re-education (Smith et al. 2009).

All exercises will be shown to you by your physiotherapist. Ensure you do three sessions of exercises per day (either standing exercises or bed exercises in one session).



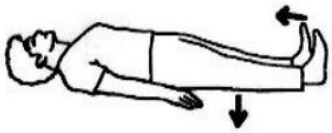
Static Gluts:

Lying on your back.

Squeeze buttocks firmly together.

Hold for 5 seconds then relax.

Repeat 10 times.

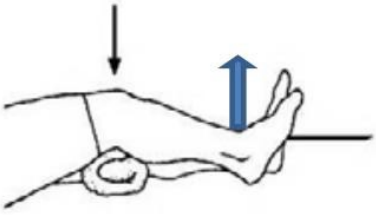


Static Quads:

Lying on your back with legs straight.

Push your knees down firmly against the bed. Hold 5 seconds then relax.

Repeat 10 times.



Inner range Quadriceps:

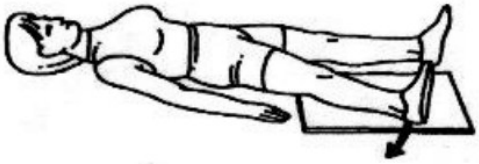
Lie or sit and place a rolled up towel under the knee of your operated leg. Point your toes to the ceiling and lift the foot to straighten the leg. Keep the knee on the roll.

Hold for 5 seconds. Lower slowly.

Hip Flexion:

Lay on your back with a plastic bag under your leg. Bend and straighten your hip and knee by sliding your foot up and down the bag.

Repeat 10 times.



Hip Abduction:

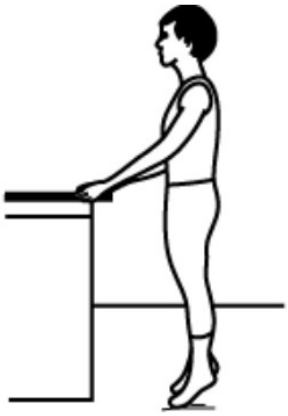
Lying on your back with a plastic bag under your leg.

Bring your leg to the side and then back to mid position.

Repeat 10 times.

Standing Exercises:

Please ensure you do these exercises holding onto a stable support with both hands.

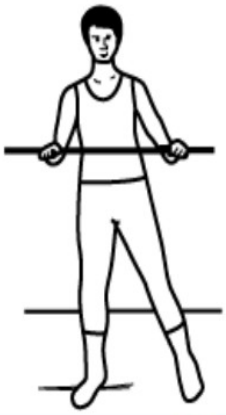


Heel Raises:

Stand up straight and hold onto something secure.

Raise your heels off the floor – coming onto your toes and then gently lower back down again.

Repeat 5 times.



Hip Abduction

Stand up straight and hold onto something secure.

Take your operated leg out to the side and slowly back in again.

Keep your foot in a straight line.

Do not turn it out to the side.

Keep your body straight; do not lean to the side.

Repeat 5 times.

You matter most

Figure 5 Example of exercises prescribed following hip replacement surgery

(Harrogate and District NHS Foundation Trust 2017)

Other exercise-based interventions have been investigated following hip replacement for several years, with the aim of counteracting muscle weakness, and enhancing recovery, without finding superiority of one exercise regime over another (Bandholm et al. 2018). A systematic review completed in 2009 found that insufficient evidence exists to establish the effectiveness of exercise following hip replacement for osteoarthritis (Minns Lowe et al. 2009). The authors found eight studies comparing physiotherapy exercises to standard care following discharge from hospital after hip replacement surgery for the treatment of hip osteoarthritis. The studies varied in their methodology and objectives, with some aiming to improve range of motion and strength (Sashika et al. 1996; Jan et al. 2004) and others targeting strength, postural stability and functional exercise (Suetta et al. 2004a). Treatment included: aerobic dance routines, individualised physiotherapy treatment, group training, supervised strengthening sessions and supervised exercise sessions combined with home exercise (Minns Lowe et al. 2009). The authors concluded that it was not possible to establish the extent to which post-discharge physiotherapy is effective in terms of improving function, quality of life, mobility, range of hip motion and muscle strength from the available evidence.

More recently, postoperative exercise has demonstrated some benefit to walking speed, pain and length of hospital stay when compared to standard care or no treatment in a meta-analysis including ten studies of 441 patients who had undergone hip replacement surgery (Wu et al. 2019). However, the exercise intervention varied in type, frequency, duration and follow up time, and therefore no further conclusions could be drawn about an optimal exercise protocol post-surgery. Interventions included resistive exercise, flexibility and strengthening interventions and treadmill training, with resistive exercise demonstrating greater benefits to walking speed than non-resistive exercise (Wu et al. 2019). Postoperative exercise was associated with an increase of the walking speed by 0.15 m/s when compared to standard care (weighted mean difference (WMD) 0.15; 95% confidence interval (CI) 0.08, 0.22; p =0.000) (Wu et al. 2019). In addition, patients who exercised postoperatively increased their Harris hip score and abduction strength when compared to the control group (Wu et al. 2019). Pain and length of stay were also lower in the exercise, however, no differences were found in postoperative physical activity levels (Wu et al. 2019).

There has been some evidence to suggest the use of progressive, home-based resistance training may be beneficial post hip replacement (Skoffer et al. 2015; Okoro et al. 2016) but the effect on muscle strength and functional capacity are reported to be minimal. Supervised, inpatient rehabilitation has been compared to unsupervised, home-based training programmes, with similar effects reported on outcomes such as hip abductor strength, gait speed and cadence (Coulter et al. 2013; Austin et al. 2017; Coulter et al. 2017). Higher intensity rehabilitation programmes are thought to ameliorate postoperative deficits in muscle strength (Bandholm and Kehlet 2012), however the underlying

mechanisms for this decreased muscle strength are still to be elucidated, and further investigation is required to inform best-practice rehabilitation techniques (Bandholm et al. 2018).

The most recent meta-analysis in this area evaluated both pre and postoperative exercise and their outcomes on hip replacement surgery (Saueressig et al. 2021). Thirty-two RCTs with 1,753 patients were included in the qualitative synthesis, and 26 studies with 1,004 patients were included in the meta-analysis. Postoperative exercise training was not associated with improvements to self-reported function at four weeks, 12 weeks, or 26 weeks postoperatively. Similarly, preoperative exercise interventions were not associated with improvements to self-reported function compared to the control group at the 12 week or 12 month follow ups or improvements to length of stay.

2.7 Rehabilitation issues to be addressed

The benefits of exercise on various systems of the body are well established. Strength training confers unique benefits to the musculoskeletal system for those with health disorders and in healthy individuals (Maestroni et al. 2020). In older adults, strength training is an effective strategy for counteracting muscle weakness, frailty, age-related intramuscular adipose infiltration, risk of falls, reduction in muscle cross sectional area and a decline in physical function. These benefits occur due to the ability of strength training to counteract age-related changes in muscle (sarcopenia) and central nervous system functions (Moore et al. 2020).

It is therefore surprising to see the volume of evidence that concludes pre and postoperative exercise have little effect on recovery from hip replacement surgery. It is possible that individuals with end-stage hip osteoarthritis may not be able to tolerate the recommended dosage of strength exercise required to induce musculoskeletal benefits (Almeida et al. 2020). This exercise load may exacerbate pain and therefore it is important to consider alternative exercise interventions that can address muscle weakness and are tolerable to the patient, such as NMES. On the other hand, it is possible that the exercise dose prescribed in the available studies is not sufficient to evoke strengthening effects. Other potential explanations include: i) high levels of heterogeneity across exercise programmes included in systematic reviews; ii) inadequate exercise type; iii) low compliance to the exercise programme, iv) not personalising the exercise intervention to suit individual characteristics; or v) not progressing exercise dose. It is perhaps a combination of these explanations precluding the developments in pre and postoperative rehabilitation. Nonetheless, one thing is clear, no intervention is yet to solve the overall problem of limited functional recovery following hip replacement surgery.

2.8 Chapter summary

Total hip replacement is a clinically successful surgical intervention for the treatment of end-stage hip osteoarthritis. The procedure has seen significant changes since it was first used in clinical practice, and the development of enhanced recovery programmes has reduced hospital length of stay and the

incidence of postoperative complications. However, the role of the pre and postoperative exercise interventions is still not fully understood in relation to improvement of mobility and physical function, and current rehabilitation practice is considered ineffective. The target of research is now to enable a patient to return to their pre-osteoarthritis levels of function and physical activities. Thus, there is a need to consider which modalities of physiotherapy and rehabilitation are feasible and can be effective for improving muscle hypertrophy within the preoperative and immediate postoperative stages of the surgical journey, where pain limits voluntary exercise. NMES may be a suitable treatment modality to address the issues raised with current practice and voluntary exercise, given its ability to activate muscles, without increasing the load on a painful joint, and is discussed further in Chapter 3. In addition, Chapter 3 summarises the current evidence for NMES for muscle strengthening purposes and explores how it may be suitable to apply to individuals with hip osteoarthritis, who may require treatment with hip replacement surgery.

Chapter 3. Literature review – Current evidence in neuromuscular electrical stimulation

3.1 Chapter introduction

In addition to voluntary activation, muscles can be contracted using electrical stimulation, which can offer advantages to preserve or restore skeletal muscle mass following periods of atrophy due to pain or immobilisation, without causing pain through mechanical loading. The broad aim of this research is therefore to explore the feasibility of NMES to improve muscle weakness in adults with hip osteoarthritis, who may undergo hip replacement surgery, with an aim of providing recommendations for future research and clinical care. This chapter discusses the mechanisms behind muscle hypertrophy, physiological considerations when prescribing NMES, and includes a literature review to summarise the current evidence for NMES for strengthening purposes in lower limb orthopaedic populations.

3.2 Definitions

The meaning of the generic term 'electrical stimulation' is complicated by the expanding use of electrical stimulation, for example, some investigators may apply it to strengthen weakened muscles and also to investigate promoted functional recovery (Watson 2008). Although the Clinical Electrophysiology Section of the American Physical Therapy Association (APTA) established unified terminology for clinical electrical currents in 1990 (APTA 1990), they are not widely adopted and are often used interchangeably in research (Watson 2008). Moreover, these definitions are somewhat outdated now, given the changes in equipment and recent modifications to traditional waveforms (Nussbaum et al. 2017).

There are several different methods of applying electrical current which include: electrical muscle stimulation (EMS), neuromuscular electrical stimulation (NMES), transcutaneous electrical nerve stimulation (TENS) and functional electrical stimulation (FES) (Doucet et al. 2012). Whilst the name of the stimulation often reflects the intended use or characteristics of the stimulation, almost all stimulators work transcutaneously through surface electrodes to excite nerves. Where the muscle is innervated by a motor nerve, the NMES term is appropriate, and where a muscle is denervated and requires direct muscle fibre activation through electrical stimulation, EMS is the appropriate term. NMES is typically used interchangeably with EMS (Doucet et al. 2012) and is often provided at sufficiently high intensities to produce muscular contraction (Watson 2008). FES, also termed functional neuromuscular stimulation (FNS) (Watson 2008), is the production of movement to produce or assist a functional task, whereas TENS machines are typically used for the purpose of modulating pain.

3.2 Muscle physiology

3.2.1 Muscle activation

During voluntary muscle contraction, muscles receive an electrical signal from the central nervous system through motor nerve cells that connect with individual muscle fibre. During electrical muscle stimulation, a stimulation pulse is delivered through the electrode that causes depolarisation of the motor nerve and this elicits a nerve impulse that causes a muscle contraction. At the positive electrode (also termed "anode"), positive ions are repelled, while negatively charged ions are attracted (Benton 1981). The negative electrode (also termed "cathode") attracts the migrating positive ions and repels the negative ions, thereby a current of ions is created, and driven into the stimulated fibre beneath the positive electrode, and out of the fibre at the negative electrode, causing excitation of nerve and muscle (Benton 1981). When an action potential is generated in a motor neuron, a muscle is stimulated, and calcium ions (Ca2+) are released. CA2+ binds to troponin, shifting the actin filaments, which exposes binding sites (Kuo and Ehrlich 2015). Myosin heads then form a cross-bridge with actin within the muscle cell that is broken by adenosine triphosphate (ATP) (Squire 2012). ATP hydrolysis causes the myosin heads to change orientation, causing them to bind to the actin filament before returning to their original conformation (DiCapua 2014). This repositioning of the myosin heads move the actin filaments towards the centre of the sarcomere, and this sliding of actin along myosin shortens the sarcomere, causing a muscle to contract, in what is called the sliding filament theory (Squire 2012).

Several factors influence whether a stimulating current delivered through electrodes is sufficient to cause neural excitation. For example, skin, adipose tissue, or bone may impede current flow, and therefore influence the outcome of stimulation. In addition, the size and orientation of the electrodes, and the parameters of the electrical stimulus (described further in section 3.2.5) will largely affect the physiological response (Benton 1981).

3.2.2 Muscle hypertrophy

Hypertrophy and hyperplasia are the two mechanisms used to explain how muscle growth occurs. Hypertrophy refers to an increase in size of individual muscle fibres, whereas hyperplasia refers to an increase in the number of muscle fibres. Hypertrophy is considered the major mechanism, with hyperplasia contributing much less to the muscle growth process. Three primary factors are responsible for exercise induced muscle hypertrophy: mechanical tension, muscle damage and metabolic stress (Schoenfeld 2010). In traditional resistance training programmes, the majority of exercise-induced hypertrophy occurs from a parallel increase in sarcomeres and myofibrils (Tesch and Larsson 1982). When skeletal muscle is subjected to an overload stimulus, it causes perturbations in myofibers and the related extracellular matrix (Schoenfeld 2010). This causes a chain of myogenic events that ultimately leads to an increase in the size and volume of the myofibrillar contractile

proteins actin and myosin, and the total number of sarcomeres (Schoenfeld 2010). This subsequently augments the diameter of individual fibres and therefore results in an increase in muscle cross sectional area (Toigo and Boutellier 2006).

Two mechanisms have been suggested to explain the training effects seen with NMES (Lake 1992). The first proposes that augmentation of muscle strength through NMES may occur in a similar manner to that of voluntary exercise, if it is prescribed with repetitions of high external load, and a high intensity of muscle contraction (Lake 1992). The second mechanism suggests that strength gains are a result of a reversal of voluntary recruitment order with a selective augmentation of type II muscle fibres, which have a higher specific force than type I fibres, which in turn increases the overall strength of the muscle (Lake 1992).

3.2.3 Motor unit recruitment

Motor unit involvement during NMES is considerably different to that of voluntary activation. In voluntary contractions, studies have demonstrated that slower-contracting motor units are recruited first in both reflex and voluntary movements involving low tensions and that larger, faster motor units are activated with bursts of rapid firing (Milner-Brown et al. 1973). It has been suggested that a change in neural input with electrical stimulation can alter the muscle response, whereby there is a reversal in recruitment order, meaning faster motor units are recruited prior to slow. This theory has largely been based upon two findings: i) that the axons of the larger motor units have a lower excitability threshold, and ii) data to demonstrate increased fatigue with NMES compared to voluntary activation (Gregory and Bickel 2005). However, as some studies have shown that nerve recruitment is random in that electrical stimulation is as likely to excite a muscle fibre connection to a type 1 fibre as a type II fibre (Jubeau et al. 2007), this theory has been challenged (Bickel et al. 2011). An alternative theory has been proposed, suggesting that motor unit recruitment during NMES reflects a nonselective, spatially fixed, and temporally synchronous pattern rather than in a reversal of the physiological voluntary recruitment order (Gregory and Bickel 2005).

During voluntary actions, the temporal recruitment of motor units is quite asynchronous, while it is imposed by the stimulator in a synchronous manner during NMES (Adams et al. 1993). Regarding spatial recruitment, constant intensity NMES imposes a continuous contractile activity to the same group of superficial muscle fibres, which diminishes proportionally with an increased distance from the electrode (Vanderthommen et al. 2000). Where current intensity is progressed, new fibres located at a greater distance from the electrode can be depolarised while superficial ones maintain their contractile activity despite neuromuscular transmission-propagation failure (Zory et al. 2005). Overall, this superficial, incomplete, asynchronous, and nonselective pattern may limit the force evoked by the stimulation and increase the rate and amount of muscle fatigue (Spector et al. 2016). Adams et al. (1993) proposed a formula to predict the activated muscle cross-sectional area in relation

to NMES training intensity (Adams et al. 1993). This formula suggests that the amount of muscle cross-sectional area activated during NMES is disproportionate to the training intensity prescribed. For example, if training at an intensity of 40-60% MVC, the amount of activated cross-sectional area would be 29-43% (Figure 6), forming a limitation of NMES when compared to voluntary exercise, as only a limited portion of the target muscle may be trained (Maffiuletti 2010),

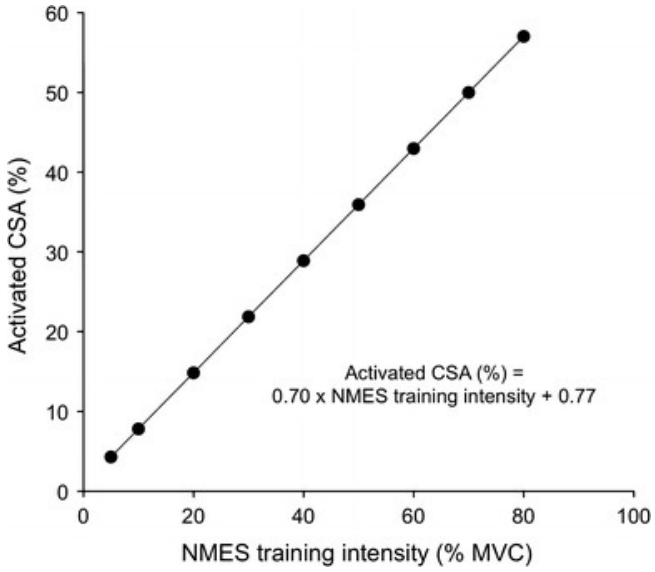


Figure 6 Quadriceps muscle cross-sectional area activated by NMES predicted using NMES training intensity (% of MVC)

(Maffiuletti 2010)

To overcome this limitation, Maffiuletti (2010) recommends strategies to maximise spatial recruitment while using NMES:

1. Increase stimulation intensity wherever possible by user, to depolarize deeper nerve fibres, thereby causing a greater muscle contraction.
2. Move electrodes after a series of contractions so the population of superficial fibres activated by NMES is changed.
3. Alter muscle length by manipulating joint angle during contraction to vary the position of muscle fibres.

The recruitment pattern of NMES offers some advantages, especially for those with impaired muscles, such as elderly individuals and orthopaedic patients who cannot perform high intensity voluntary contractions because of pain, surgery, or impaired activation (Maffiuletti 2010). NMES can be used to recruit specific muscle fibres, bypassing the need to volitionally activate muscle fibres, and may result in increased muscle strength and endurance, improved oxidative capacity and induce a

shift toward a slower muscle phenotype (Petterson and Snyder-Mackler 2006; Kim et al. 2010; Gondin et al. 2011). Furthermore, some evidence suggests NMES can modify the excitability of specific neural paths at the spinal cord and cortical levels, leading to neural adaptions rather than just muscle hypertrophy (Hortobagyi and Maffiuletti 2011).

3.2.4 Strength and endurance training

Exercise is generally categorised into endurance or power/strength activities. Endurance exercise is typically performed against a relatively low load over a long duration, whereas strength exercise is performed against a relatively high load for a short duration (Hughes et al. 2018). However, endurance and strength training in isolation are rare, with most activities combining endurance and strength to a certain extent, in what is known as concurrent exercise (Hughes et al. 2018). Furthermore, research has found that short, high-intensity exercise can lead to endurance adaptions, and low-load exercise that approaches failure can lead to strength adaptions (Hughes et al. 2018). Nonetheless, both voluntary exercise and NMES can be prescribed to target endurance or strength adaptions and must be considered when designing NMES protocols.

3.2.5 NMES parameters

When prescribing NMES interventions, there are several parameters that can be modified to affect the desired outcome. For example, stimulation frequency refers to the pulses produced per second during stimulation and can be modified to influence the outcomes of treatment. In addition, “on” and “off” time, also described as the “duty cycle”, is an important parameter to influence neuromuscular fatigue. Much like voluntary exercise, the “on” cycle represents the period of time where the stimulator is delivering a train of electrical pulses, and the “off” time is a period of rest and recuperation (Benton 1981). In muscle strengthening, electrical stimulation induces a high level of muscle fatigue, and therefore a lower frequency of stimulation (≈ 20 Hz) may be prescribed in an attempt to produce a smooth contraction with low force levels, without increasing muscle fatigue (Bhadra and Peckham 1997). When combined with using long on and short off times, to encourage a transition in muscle fibre phenotype from fast twitch properties to slower, fatigue resistance properties, muscle endurance can be improved. Where an increase in maximal strength or power is the desired outcome, a higher frequency of stimulation (40-75 Hz) may be prescribed to reach a higher level of evoked force. Furthermore, stimulation amplitude, or intensity, of the current pulse, and it’s duration (or pulse width), must be adequate to meet or exceed the threshold of excitability of the stimulated tissue, in order to create a stimulation response (Benton 1981). However, issues can arise if a stimulation intensity sufficient to evoke a muscular contraction cannot be tolerated by the user and is explored in individuals with hip osteoarthritis in Chapter 5. Definitions of NMES parameters relevant to this research are adapted from the work by Nussbaum et al. (2017) in Table 2. Other parameters can be manipulated in electrical stimulation, such as charge, charge density and waveform,

however these definitions were not included in Table 2 as it was not possible to modify these parameters in the stimulator used in this research.

NMES parameter	Definition
Frequency (pulse rate, Hertz (Hz) or pulses per second (pps))	The number of pulses in one second.
Phase and pulse duration (microseconds)	The time elapsed from when the current (or voltage) leaves the isoelectric (zero) line until it returns to baseline. It includes both positive and negative phases when the pulse is biphasic as well as any interphase interval.
Pulse amplitude (millivolts or milliamperes)	The magnitude of the current or voltage deviation from zero or isoelectric line.
On time	The time over which a series of pulses is delivered.
Off time	The time over which the stimulator automatically cycles off and no current is delivered. For example, a period of rest between muscle contractions.
On:off ratio	A ratio of the on time and off time of each cycle.
Ramp up time	The amount of time it takes for the stimulating current to reach the set amplitude of an on cycle, normally 1-2 seconds. This is normally counted within the total on time.
Ramp down time	The amount of time it takes for the stimulating current to return to zero intensity at the end of each on cycle, normally 1-2 seconds. This is normally included in the total off time.

Table 2 Electrical stimulation parameters
(Nussbaum et al. 2017)

3.3 Methodology

The first study conducted as part of this thesis was a literature review, which was performed to summarise and evaluate the available evidence for NMES for strengthening purposes in patients with hip osteoarthritis undergoing hip replacement, to inform the design of subsequent research endeavours. Specifically, the literature review sought to identify studies that had tested an intervention of NMES of surgical or non-surgical hip osteoarthritis patients for strengthening purposes pre- or post-operatively, with the aim of answering the following questions:

1. What effect does NMES have on the muscle strength or endurance of lower limb orthopaedic patients?

2. What NMES parameters and protocol are used to strengthen muscles in lower limb orthopaedic patients?

While a systematic review was originally planned, once the search begun, it was clear that the limited available studies would prevent the completion of a systematic review. It was therefore decided to complete a broader scoping review of the literature, so that related research outside of the target population could be used to inform later stages of this research, and thus related research in knee osteoarthritis and hip fracture was included. While systematic reviews are the gold standard methodology to summarise available evidence, a scoping review can provide a more complete overview of all research related to a topic (Pham et al. 2014) and therefore was considered appropriate for this research. To ensure complete reporting, the methodology of this review is reported with guidance from the PRISMA extension for scoping reviews in following sections of this chapter (Tricco et al. 2018).

3.3.1 Eligibility criteria

Studies were included in the results synthesis if they were investigating an intervention of NMES in isolation, applied for strengthening purposes, in a hip or knee osteoarthritis population. Furthermore, the review included studies in patients receiving a hip replacement for the treatment of a hip fracture. As this review sought to gain a broad understanding of NMES protocols and their potential benefits, or limitations, studies were not limited to specific outcome measures or comparative interventions. In addition, both surgical and non-surgical patient populations were eligible for inclusion, regardless of whether NMES was applied conservatively, preoperatively, or postoperatively. All study types were included, except for study protocols, as although RCTs are the gold standard methodology for conducting research, the limited and heterogenous evidence available meant a broader approach was required to inform future stages of this research. Furthermore, in addition to primary searching, secondary searching was undertaken, whereby the reference lists of the yielded studies were scanned for eligible studies, to reduce the risk of relevant studies being missed. Studies that had applied NMES for purposes other than muscle strengthening were excluded (for example, NMES to increase blood flow). The predetermined eligibility criteria are described in accordance with the PICOS criteria (Higgins and Green 2013) in Table 3.

Inclusion	Exclusion
Population	
• Non-surgical, or surgical patients with hip or knee osteoarthritis • For surgical patients, all forms of fixation, surgical approaches, and types of prosthetic bearing surfaces. • Hip fracture patients • Adults aged 18 years or older	• Studies on animals
Intervention	
• Electrical muscle stimulation (EMS), neuromuscular electrical stimulation (NMES), or functional electrical stimulation (FES) applied for strengthening purposes independently or with only standard care. • Performed conservatively, pre or postoperatively • Performed in an inpatient, outpatient, or home/community care setting.	• Electrical muscle stimulation (EMS), neuromuscular electrical stimulation (NMES), or functional electrical stimulation (FES) applied for non-strengthening purposes. • Any other form of electrical stimulation. • Electrical stimulation performed with another intervention with no separate analysis.
Comparison	
• All considered	
Outcome measures	
• All considered	
Study type	
• Randomised or non-randomised trials • Systematic reviews and meta-analyses Observational cohort studies • Case-studies • Retrospective analyses • Published in the English language • Access to full text	• Study protocols

Table 3 Inclusion and exclusion criteria for scoping review

3.3.2 Information sources

A web-based literature search was initially completed in March 2018, and published in part in 2019 (Burgess et al. 2019). It was updated and expanded in September 2022, with the findings of the original review and updated search presented here. The databases sourced included the Cochrane Library, Medline Complete, PubMed and CINAHL (The Culmative Index to Nursing and Allied Health Literature), accessed through Bournemouth University's online library.

3.3.3 Search strategy

A broad search strategy (Figure 7) was designed to yield studies of NMES interventions, prescribed for strengthening purposes, in individuals with hip or knee arthritis, or undergoing lower limb orthopaedic surgery. The search strategy combined disease and procedure specific terms, with key words related to electrical stimulation, and terms to identify studies on muscle strengthening. No methodological search terms were used, given that all study types were considered for inclusion.

[Title/Abstract] "hip arthritis" OR "knee arthritis" OR "hip osteoarthritis" OR "knee osteoarthritis" OR "hip replacement" OR "knee replacement" OR "hip arthroplasty" OR "knee arthroplasty" OR "joint replacement" OR "joint arthroplasty" OR "hip fracture" OR "neck of femur fracture" OR "nof fracture" OR "FNOF" AND [Title/Abstract] "electrical stimulation" OR "electrical muscle stimulation" OR electrostimulation OR electric stimulation AND [Title/Abstract] "muscle strength" OR "muscle mass" OR "muscle atrophy" OR "muscle endurance" OR strengthening OR rehabilitation OR weakness

Figure 7 Search strategy

3.3.4 Selection of sources of evidence

All titles and abstracts of the yielded results were initially checked for relevance. Once irrelevant and duplicate studies had been removed, the remaining articles underwent a full-text appraisal to ensure that the studies were of good methodological quality, that their findings were significant, and that they were evaluating an NMES device for strengthening purpose in a lower limb orthopaedic population.

3.3.5 Data extraction

Data were extracted from the included studies into extraction sheets developed in Microsoft Excel. The following data were extracted: i) NMES parameters; ii) NMES training protocol; iii) outcome measures of interest.

3.3.6 Results synthesis

Due to the limited and heterogenous studies available, data were analysed from individual studies using a narrative synthesis approach. Where available, differences in outcome measure means were the primary summary measure.

3.3.7 Quality assessment

Giving the scoping nature of this review, it was not considered appropriate to conduct a quality assessment the studies discussed in the results synthesis (Arksey and O'Malley 2007). However, the PEDro (Physiotherapy Evidence Database) scale was used to grade the methodological quality of the studies conducted amongst a hip osteoarthritis population due to its suitability to measure the methodological quality of clinical trials (de Morton 2009). The PEDro scale is described in detail, along with the results in the published part of this review (Burgess et al. 2019).

3.4 Results

3.4.1 NMES in hip osteoarthritis

The search identified two studies that had investigated an intervention of NMES in patients with hip osteoarthritis who had undergone hip replacement surgery, and these are summarised and critiqued in a published article, including an assessment of quality (Burgess et al. 2019). The following section of this chapter has been previously published as, Burgess, L.C., Swain, I.D., Taylor, P. and Wainwright, T.W., 2019. Strengthening quadriceps muscles with neuromuscular electrical stimulation following total hip replacement: a Review. Current Physical Medicine and Rehabilitation Reports. 7. 275-283.

One study has investigated the effects of unilateral NMES on the operated side following hip replacement compared to standard home-based rehabilitation or unilateral resistance training of the operated side in elderly patients (Suetta et al. 2004b). The patients received one hour of stimulation a day for 12 weeks to the quadriceps muscles, at a pulse rate of 40 Hz, a pulse width of 250 μs and each stimulation package lasted for 10 s, followed by 20 s of rest. During the first and last two seconds of stimulation, the amplitude increased and decreased gradually respectively. Resistance training included daily knee extension exercises (3 × 10 repetitions) in the seated position with sandbags strapped to the ankle during hospitalisation. As soon as possible, training was performed on adjustable leg press and knee-extension machines. The protocol included a 10-min warm-up on a stationary bike, seated knee extensions and leg presses performed in the supine position. Training intensity was progressively increased in intensity from 20-repetition maximum (RM) (~ 50% of 1 RM) the first week to 15 RM (~ 65% of 1 RM) during weeks two to four to 12 RM (~ 70% of 1 RM) during weeks five to six and finally to 8 RM (~ 80% of 1 RM) the last 6 weeks. Data were analysed between training groups and from pre to post intervention.

Mean ± standard error length of stay was shorter for the resistance training group (10.0 ± 2.4 days) than the electrical stimulation group (12 ± 2.8 days) and the standard rehabilitation group (16.0 ± 7.2 days) (p <0.05). Resistance training increased maximal gait speed by 30% (p <0.001), stair climbing performance by 28% (p <0.005) and sit-to-stand score by 30% (p < 0.001) from the pre-intervention assessment to the post-intervention assessment. Electrical stimulation increased maximal gait speed by 19% (p <0 .05), stair climbing performance by 21% (p < 0.001) and sit-to-stand score by 21% (p <0.001) from baseline to the post-intervention assessment. No improvements were seen in these measures for the group receiving standard, home-based rehabilitation. Quadriceps muscle cross-sectional area of the operated leg decreased by 13% at 5 weeks post-surgery in the standard care group (p <0.05) and remained 9% below baseline values at 12 weeks following surgery (p <0.05). In the resistance training group, cross-sectional area of the operated leg was unaltered at 5 weeks post-surgery and increased by 12% from baseline values to 12 weeks following surgery (p < 0.05). In the electrical stimulation group, cross-sectional area of the operated side decreased from baseline by 4% at 5 weeks following surgery (p <0.05) and increased by 7% from 5 weeks to 12 weeks following surgery (p <0.05). The non-operated side was unaffected in all three groups. Between group comparisons demonstrated that the changes in cross-sectional area for resistance training were greater than electrical stimulation (5 weeks: p = 0.04, 12 weeks p < 0.001) and standard rehabilitation (5 weeks: p = 0.002, 12 weeks: p <0.001). Peak torque improved on the operated leg for the resistance training group by 28% at 60°/s (p <0 .001) and 22% at 180°/s (p <0.05) at 12 weeks following surgery, but there were no changes on either leg at any time for the electrical stimulation and standard care groups (Suetta et al. 2004b). A second evaluation of the same participants included measures to evaluate muscle morphology, architecture, and function (Suetta et al. 2008). After twelve weeks, the authors found that resistance training led to improvements in maximal dynamic muscle strength, muscle fibre area, muscle fibre pennation angle, muscle thickness and stair walking power. Interestingly however, there were no increases to any measures in the participants receiving electrical stimulation or standard rehabilitation (Suetta et al. 2008).

Low-frequency electrical stimulation of the quadriceps and calf muscles, in addition to conventional physiotherapy, has been compared to conventional physiotherapy alone following hip replacement surgery in one study (Gremeaux et al. 2008). Stimulation was applied to the quadriceps and calf muscles bilaterally using two portable dual-channel stimulators. Each delivered a 10-Hz biphasic current, with a pulse width of 200 μs and each cycle was on and off alternatively for 20 seconds. As the rehabilitation intervention progressed, the stimulation intensity applied to each muscle was increased to the maximum value tolerated by the patients. The stimulation occurred for a 1-hour session, 5 days a week for 5 weeks in addition to 2 hours of physiotherapy. All included participants were evaluated at baseline, and 45 days later. Low-frequency electrical muscle stimulation of the quadriceps and calf muscles in addition to conventional physiotherapy, in elderly subjects (mean age

78 years) was well tolerated and led to a significant increase in muscle strength in the operated limb from baseline to 45 days later. There was a significant increase from baseline in maximal isometric strength of the knee extensors on the operated (77% increase ($p < 0.01$)) and non-operated (15% increase ($p < .005$)) sides in the electrical stimulation group, and in the operated limb of the control group (23% increase ($p < 0.05$)). When compared to the control group, the improvement in strength was significantly greater for the electrical stimulation group for the operated limb ($p <0 .05$) but not for the non-operated limb. A post-hoc analysis showed significant improvement in pre-post change of functional status and degree of independence (as measured by the Functional Independence Measure) only in the electrical stimulation group, and not the control (21% increase vs 16% increase, respectively, ($p <0.05$)). Although there were no significant differences in walking speed or length of stay between the electrical stimulation and control groups, the stimulation was advocated as a safe and effective adjunct therapy to standard care for hip replacement patients (Gremeaux et al. 2008).

3.4.2 NMES in knee osteoarthritis

Although limited in hip osteoarthritis, the research evidence evaluating NMES in patients with knee osteoarthritis is better established. While osteoarthritis of the hip and knee should be treated individually, there are similarities between patient groups and therefore it is useful to draw upon the available evidence for NMES for improving strength in patients with knee osteoarthritis.

In non-surgical knee osteoarthritis patients, a meta-analysis of nine studies (409 participants) concluded that inconsistent evidence exists regarding the impact of NMES on measures of pain, function and quadriceps femoris muscle strength (Giggins et al. 2012). However, the results from a pooled analyses found that NMES improved self-reported pain and function, but not objective measures of function (Giggins et al. 2012). It should be noted however that questions have been raised regarding the methodology of this work, suggesting there was a lack of consistency amongst the NMES interventions included in the analysis (Li et al. 2014). The first review to provide standardised clinical treatment parameters for NMES to improve strength and pain in patients with knee osteoarthritis was published in 2020 (Novak et al. 2020). Nine RCTs were included, the authors recommended a frequency of at least 50 Hz and no more than 75 Hz with a pulse duration between 200 and 400 μs and a treatment duration of 20 minutes in order to achieve a successful treatment to improve muscle strength (Novak et al. 2020). This review was the first of its kind, providing an important steppingstone for future clinical work and research endeavours involving NMES.

A Cochrane review conducted in 2008 and updated in 2010 sought to evaluate the effects of NMES for quadriceps strengthening pre and post total knee replacement (Monaghan et al. 2010). The authors found just two studies suitable for inclusion in the evidence synthesis and from this limited evidence, were unable to make any conclusions on the application of NMES for purposes of strengthening quadriceps pre or post knee replacement surgery. In the two included studies, no differences were

reported between the NMES and control groups for maximum voluntary isometric torque or endurance, but significantly better quadriceps muscle activation was noted in one study (Oldham et al. 1995; Stevens et al. 2003). A systematic review published in 2015 was largely in agreement with earlier work, concluding from four studies with a moderate risk of bias, and a low statistical power, that NMES is less effective than traditional rehabilitation yet may offer advantages to muscle activation in the early postoperative stage (Volpato et al. 2016). Similarly, Kittelson conducted a critical review in 2015, and found mixed evidence for the benefits of NMES, with the included studies varying considerably in regard to their methodology and dose of NMES (Kittelson et al. 2013).

More recently, a meta-analysis of six studies (496 patients) evaluated NMES use in patients undergoing knee replacement in comparison to patients in a control group and reported benefits to timed up and go, stair climb and walk test scores, particularly in those with severe muscle activation deficits (Bistolfi et al. 2018). The benefits of NMES were strongest in the first postoperative weeks/months and gradually diminished, suggesting the NMES may allow better functional recovery in the immediate postoperative phase (Bistolfi et al. 2018). A recently published randomised controlled trial of 66 participants (NMES use = 44, no NMES = 22) evaluated NMES use for quadriceps strengthening for an average of 200 minutes per week starting at postoperative week one for twelve weeks (Klika et al. 2022). NMES was prescribed at a frequency of 50 Hz, with an unusually long pulse duration of 5 ms and a current capable of causing superior patella glide or higher as tolerated. Patients using NMES experienced quadriceps strength gains at three, six- and twelve-weeks following surgery, which were significant when compared with the control group at three (p = 0.050) and six weeks (p = 0.015). In addition, improvements in timed up and go time were found when compared to the control group at six (p = 0.018) and twelve weeks (p = 0.003) postoperatively. However, no differences were observed between groups regarding range of motion, pain, length of stay, number of outpatient physiotherapy sessions, pain catastrophising score, mental component score or knee injury and osteoarthritis outcome score (KOOS) (Klika et al. 2022).

3.4.3 NMES in hip fracture

A recent systematic review evaluated the evidence for electrical stimulation to improve clinical recovery from a hip fracture (Davison et al. 2021). The review included four studies comparing interventions of electrical stimulation to no stimulation in patients following hip fracture surgery. The review included TENS interventions in addition to NMES, and therefore examined pain outcome measures in as well as leg extension power and functional measures. Three studies investigated electrical stimulation and its effect on leg extension power. The active electrode was placed proximally at point of maximal contraction (femoral nerve or vastus lateralis) and the negative electrode was positioned distally over muscle of the fractured leg in two studies (Barber et al. 2002; Braid et al. 2008).

In one study, patients receiving NMES treatment experienced significant improvements in leg extension power in both their fractured and non-fractured legs when compared to the control group at six weeks, however, at 16 weeks no significant differences existed between the groups in either leg (Barber et al. 2002). In two studies, no differences existed between groups in the fractured and non-fractured legs at six weeks and 14 weeks (Braid et al. 2008) or at seven weeks and 13 weeks following fracture (Lamb et al. 2002). Interestingly, however, some benefits were observed to usual gait speed at 13 weeks post-surgery for patients receiving NMES, when compared to the control group (mean difference: -0.13 m/s, 95% CI -0.232 to -0.009) (Lamb et al. 2002).

Several reasons were suggested for the contrasting results. The first was that perhaps a six-week intervention was not sufficient to elicit strength gains in the quadriceps muscles follow hip fracture surgery (Davison et al. 2021). Secondly, it was suggested that the parameters used in the included studies were not appropriate to elicit the desired outcome. The participants of Lamb et al. (2002) received three hours of lower-frequency (mean 8.9 Hz) NMES daily (84 hours in total), compared to 20 minutes of higher frequency (40-100 Hz) NMES 2-5 times per week in the study by Braid et al. (2008). Although it is not possible to confirm which protocol is superior, this early evidence supports the use of a lower-frequency protocol for people after hip fractures, as the lack of effect reported by Braid et al. (2008) likely represents a poor tolerance to the treatment exhibited by participants. It was estimated that participants chose an intensity that stimulated much less than 40% of their maximum voluntary contraction, which may explain the limited effect on strength gain (Braid et al. 2008). These findings differ from the guidelines proposed by Novak et al. (2021), whereby a higher frequency of between 50-75 Hz is recommended for strengthening purposes in patients with knee osteoarthritis, although these recommendations are for non-surgical patients (Novak et al. 2020).

3.5 Discussion

The aim of this scoping review was to i) examine what effect NMES has on the muscle strength or endurance of lower limb orthopaedic patients and ii) determine which NMES parameters and protocol are effective at strengthening muscles in lower limb orthopaedic patients. However, due to the limited available studies, small sample sizes, and differences in protocol design and patient demographics, it is not yet possible to determine an optimal NMES protocol for patients with hip osteoarthritis, who may require treatment with hip replacement surgery. To date, application of NMES has been limited to the postoperative phase, and NMES has been applied to the quadriceps alone (Suetta et al. 2004b), or the quadriceps and calf muscles in combination (Gremeaux et al. 2008). Emerging evidence suggests that it is possible to improve length of stay, gait speed, stair climbing performance, sit-to-stand scores, and a reduction in muscle cross-sectional area (Suetta et al. 2004b). Conversely, opposing evidence found no significant effect of NMES on length of stay or gait speed, yet benefits to knee extensor strength of the operated side, functional status, and independence (Gremeaux et al.

2008). However, the findings between the studies are not directly comparable, due to differences in protocol design and patient demographics. Both studies conclude by highlighting the potential benefits of using NMES alongside conventional physiotherapy care, however Suetta et al. believe resistance training has a greater effect on recovery (Suetta et al. 2004b; Suetta et al. 2008).

Investigations in knee osteoarthritis have sought to establish the benefit of NMES for overcoming muscle weakness and functional deficits in the non-surgical and surgical populations. Guidelines for optimal stimulation parameters to increase quadriceps strength and decrease pain have been recommended in non-surgical patients and are advocated to improve peak quadriceps torque (Novak et al. 2020). The authors provide recommendations for a stimulation frequency of between 50 and 75 Hz, and a pulse duration of between 200 μs and 400 μs, formed on the basis that they can improve pain and strength measures. In addition, the authors recommend five days of stimulation compared to three days per week (Novak et al. 2020). However, these recommendations are based on only limited evidence, and therefore should be investigated with caution.

In knee replacement surgery, the role of NMES applied to the quadriceps during recovery post-surgery has been scrutinised in several reviews, including a Cochrane review (Monaghan et al. 2010; Kittelson et al. 2013; Volpato et al. 2016; Bistolfi et al. 2018). While some benefits of NMES are highlighted regarding increased muscle activation, quadriceps strength improvement and function performance, the role of NMES is not fully understood, and an optimal NMES protocol has not yet been agreed on. All the included reviews were limited by the low number of included studies, their small sample sizes, and heterogeneity in their NMES protocols, especially regarding initiation of treatment, duration of treatment, and NMES parameters. These limitations can also be applied to the available evidence in hip fracture surgery; whereby mixed evidence for the effectiveness of NMES is attributed to differences in study protocols and low tolerance of the prescribed NMES dose by patients (Davison et al. 2021).

3.6 Limitations

This scoping review provided a broad understanding of the available evidence for NMES used for strengthening purposes in lower limb orthopaedic populations. Nonetheless, it is possible that the broad search strategy used meant some relevant studies may have been missed from the search. The depth of analysis was also restricted given the limited and heterogeneous nature of the studies yielded. While the emphasis of this scoping review was to provide a comprehensive overview of the existing literature, the absence of quality assessment in the knee osteoarthritis, knee replacement and hip fracture studies limits the strength of this synthesis. Nonetheless, the scoping review was designed to provide a broad understanding of the current evidence-base, rather than to determine the standard of the evidence.

3.7 Chapter summary

While limited, emerging evidence suggests that NMES applied to lower limb orthopaedic populations may be a feasible and effective intervention to improve muscle strength. To date, no studies have investigated the benefits of NMES in a non-surgical hip osteoarthritis population, or prior to hip replacement surgery as part of a prehabilitation programme. In addition, there is a paucity of evidence for NMES use in post-surgical hip replacement patients, with only two studies to date examining an independent intervention of NMES for strength improvement purposes. The heterogeneity in interventions and populations included in the available literature precludes the formation of guidelines for NMES parameters and dose, and therefore further work is required in this area. In addition, further work is required to understand i) if NMES is an acceptable treatment modality for patients with hip osteoarthritis, ii) if NMES is effective at improving muscle strength in this patient population and iii) whether improvements in strength can lead to meaningful changes in mobility and physical function.

Chapter 4. Strength and endurance deficits in adults with moderate-to-severe hip osteoarthritis, compared to healthy, older adults

4.1 Chapter introduction

The early stages of this research sought to learn more about which muscle groups were most affected by hip osteoarthritis, and whether it would be more beneficial to train maximal strength, or strength endurance in this population, to inform the design of an NMES intervention (Chapter 8). To effectively prescribe NMES, and other rehabilitation programmes, it is crucial to understand the underlying muscle impairment in the target population, and its relationship with physical function and disease progression. Therefore the first study of this thesis, described in section 4.4, aimed to compare lower limb maximal muscle strength and local muscular endurance in adults with hip osteoarthritis, to an age-matched control group, to inform the design of an effective NMES training protocol to address muscle weakness.

4.2 Rationale

Much like voluntary exercise, NMES parameters and application can be altered for different purposes. For example, the Odstock Medical Orthopaedic Microstim has stimulation settings aimed at improving blood flow, pain relief, general muscle conditioning, endurance training and strength/power (Odstock Medical Ltd 2020). Using the blood flow settings, it is possible to replicate a calf muscle squeeze, by using a 0.5 or 1 second burst of stimulation to stimulate the common peroneal nerve, causing dorsiflexion and activating the calf muscle pump. Endurance settings are designed to improve muscle endurance by using a low frequency to minimise fatigue, but with long on and short off times to maximise the duration of contraction and encourage a change muscle fibre property from fast to slower, fatigue resistance fibres. Power settings use a higher frequency with short bursts of high intensity stimulation to induce muscle fatigue. In hip osteoarthritis, research endeavours have sought to identify which muscle groups are most affected in terms of maximal strength and/or power (Loureiro et al. 2013). However, local muscle endurance has not been studied to the same extent, despite the physiological stimuli directed to skeletal muscle as a result of strength training and endurance training being divergent in nature (Häkkinen et al. 1995). Therefore, this study was conducted with the aim of informing the training principles to underpin the NMES intervention assessed in Chapter 8.

This study compared the strength of the knee extensors (quadriceps femoris), knee flexors (hamstrings, gracilis, sartorius, gastrocnemius, plantaris and popliteus) and hip abductors (gluteus medius, gluteus minimus, and tensor faciae latae) muscle groups, so that in combination with the findings from Chapter 5, a muscle group could be chosen as the target for the NMES intervention. While it is largely agreed that muscle weakness persists in the lower limbs of individuals with hip

osteoarthritis, as discussed in Chapter 2, there is little evidence to compare which muscle group is most significantly affected. In addition, this research sought to identify whether muscle weakness exists only in the affected limb, or both limbs, of individuals with hip osteoarthritis, so that it could be decided whether to prescribe NMES on a unilateral or bilateral basis.

The objectives of this research study are listed below:

1. To compare maximal isometric strength to muscular endurance of the affected and contralateral limbs in individuals with symptomatic hip osteoarthritis to a healthy age-matched control group.
2. To identify whether the knee extensors (quadriceps femoris), knee flexors (hamstrings, gracilis, sartorius, gastrocnemius, plantaris and popliteus) or hip abductors (gluteus medius, gluteus minimus, and tensor faciae latae) are most affected in individuals with hip osteoarthritis.
3. To identify if asymmetries exist in the lower limb strength of the affected and contralateral limbs of individuals with osteoarthritis.
4. To identify if muscle weakness translates to impairments in mobility and physical function.

4.3 Methodology

This study was an observational case-control study recruiting two groups: (i) adults aged over 60 years with a clinical diagnosis of unilateral or bilateral hip osteoarthritis and (ii) healthy adults aged over 60 years (control group) between 12th November 2019 and 15th March 2020. In a case-control study, participants who have developed a disease are identified and compared to controls who do not have that disease (Coggan et al. 2009). A case-control study was considered an appropriate design as this research sought to understand a specific population, who had been diagnosed with hip osteoarthritis. In addition, the inclusion of a control group allowed an insight into how individuals with hip osteoarthritis compare to their healthy counterparts, so that an appropriate NMES intervention could be designed to promote normal function. There were no differences between groups in terms of age, gender distribution, or activity levels, however, the BMI of the osteoarthritis group was higher than the control group. To negate this, strength scores were normalised to body weight as described in the research article in section 4.4.

The full methodology of this study is described in the research article that comprises section 4.4 of this thesis (Burgess et al. 2021c) and described in brief here. The experimental protocol was approved by the Bournemouth University Ethics Committee on 5th September 2019 (Appendix 1). Participants were recruited from the local area through online advertisement (Twitter, Facebook) and email recruitment sent to local organisations, such as the University of the 3rd Age (U3A). Those interested in the study were asked to contact the lead researcher for more information. Once an individual had

expressed an interest in taking part, they were sent a participant information sheet (Appendix 2) and consent form (Appendix 3) to consider before being invited to ORI at Bournemouth University (Bournemouth, UK) where their eligibility was checked, and their informed consent received.

Participants took part in a muscle testing session, whereby they completed a series of strength tests using a multimodal dynamometer (Primus RS, Baltimore Therapeutic Equipment, Hanover, NH) (Figure 8), functional tests as per recommendations from the Osteoarthritis Research Society International (OARSI) (Dobson et al. 2013a) and PROMs (Appendices 4 and 5). Data were collected on paper case report forms (CRFs), and later entered onto a secure, web-based data management portal (Actipath, Actipath Ltd, Poole, UK). Data were analysed to compare differences between participants with and without hip osteoarthritis, and between the affected and contralateral limb. In keeping with good practice, the ethical principles for medical research outlined in the Declaration of Helsinki were followed (World Medical Association 2018). The full methodology of this study is described according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement (von Elm et al. 2014) in section 4.4 of this thesis.

Figure 8 Primus RS dynamometer

Used with permission of the Orthopaedic Research Institute, Bournemouth University

4.4 Research article

Strength and endurance deficits in adults with moderate-to-severe hip osteoarthritis, compared to healthy, older adults.

Louise C. Burgess, Paul Taylor, Thomas W. Wainwright & Ian D. Swain

Read the article at
https://eprints.bournemouth.ac.uk/35683/

4.5 Results synthesis

This study aimed to gain an understanding of the physiological deficits common in individuals with hip osteoarthritis, to inform the design of the NMES intervention described in Chapter 8. The study found that individuals with moderate-to-severe hip osteoarthritis demonstrate significant weakness of the knee extensors, knee flexors and hip abductors when compared to their healthy counterparts. The findings suggest that knee extensor endurance may be the most considerably impaired measure, and the impact of this was demonstrated by the findings of a functional assessment, whereby people with hip osteoarthritis took considerably longer to complete the assessments of walking, stair climbing, and rising from a chair. In the control group, no asymmetries were observed in maximal strength of the knee extensors, knee flexors or hip abductors. However, in individuals with hip osteoarthritis, the affected leg demonstrated weakness of 10% in the knee extensors and 35% in the hip abductors when compared to the contralateral limb. No asymmetries were observed in the knee flexors in terms of maximal strength in those with osteoarthritis. Similarly, no asymmetries were observed between the isotonic endurance of the knee extensors of the affected and contralateral legs of the participants with hip osteoarthritis ($p = 0.26$) or left and right legs of the control group ($p = 0.12$). In the osteoarthritis group, isotonic muscular endurance of the knee extensors in the affected leg was 70% lower than the right leg of the control group ($p = 0.001$). Likewise, the knee extensors of the contralateral leg were exhausted prematurely when compared to the right leg of the control group (62%) ($p = 0.005$), suggesting bilateral endurance deficits. Both comparisons yielded large effect sizes ($d = 1.41$ and 1.17, respectively).

4.6 Discussion

It is well documented that adults with hip osteoarthritis exhibit generalised muscle weakness of the affected limb, underpinned by a combination of muscle atrophy, reduced muscle density, and muscle inhibition, when compared to healthy adults, however, to date, research has focused on maximal strength outcomes rather than endurance capacity (Loureiro et al. 2013). To effectively prescribe NMES interventions, it is crucial to understand the underlying muscle impairment in the target population, and its relationship with physical function and disease progression. The findings from the maximal strength assessment described here are consistent with the existing evidence-base, suggesting that the hip abductors may be most significantly affected muscle group, followed by the knee extensors and the knee flexors, and therefore designing rehabilitation interventions to target these muscle groups may be of benefit. In addition, muscle strength asymmetries exist in adults with moderate-to-severe hip osteoarthritis, but not in earlier stages of the disease (Loureiro et al. 2018), and therefore it may be beneficial to prescribe bilateral strengthening exercise.

The main and novel finding of this study was that the endurance capacity of the knee extensors was markedly lower in both the affected (70%) and contralateral sides (62%) of the hip osteoarthritis group when compared to the control group. Knee extensor endurance has important clinical

implications due to the significant role of the quadriceps femoris endurance for functional capabilities during activities of daily living, such as walking, rising from a chair, and climbing stairs. In addition, deficits in knee extensor endurance have been associated with a significant and linear increase in persistent lower limb limitation and mortality (Roshanravan et al. 2017) and cardiovascular risk factors (Vaara et al. 2014). The findings from the functional assessment further highlight the need to train endurance in the lower limbs of individuals with hip osteoarthritis, given that it took this group twice as long to complete the stair negotiation test, 40% longer to complete the 40 m walk test and they had a 35% lower sit-stand performance.

These findings are important to inform the design of the NMES intervention, described in Chapter 8. Maximal strength involves exerting a maximum amount of force for a short period of time whereas muscular endurance is the ability of the muscle or muscle group to sustain repeated contractions against a load for an extended period of time (Kell et al. 2001). While maximal strength is important to help with explosive activities, lower limb endurance has important clinical implications due to its significant role in functional capability during activities of daily living, such as walking, or stair climbing. Training with low repetitions and high resistance favours adaptions for strength, power, and hypertrophy, whereas training with high repetitions and low resistance increases muscular endurance and appears more suitable for submaximal, prolonged contractions (Campos et al. 2002). When prescribing NMES, parameters can be modified to favour maximal strength or endurance outcomes. For example, to improve muscle endurance, NMES may be prescribed at a lower frequency of stimulation but using long on and short off times to induce a change in muscle fibre properties from fast to slow. Where an increase in maximal strength or power is the desired outcome, a higher frequency with short bursts of high intensity may be used to evoke a higher level of evoked force and induce muscle fatigue. Given the concern that high-intensity or high-load strength training may increase pain and joint stress for those with osteoarthritis (Latham and Liu 2010), in addition to the function and endurance deficits observed in the present study, endurance training may be the most suitable training modality in the hip osteoarthritis population.

4.7 Limitations

As discussed further in the published paper that comprises section 4.4, and Chapter 6, this research was limited by its early closure due to the Covid-19 pandemic, and the failure to reach the sample size estimates calculated ahead of the study starting. However, a post-hoc power analysis suggested that it was only knee extension MVIC that was underpowered. The cross-sectional design of the study did not allow us to evaluate whether muscle weakness is a cause or consequence of hip osteoarthritis. Nonetheless, the methodology chosen was the most suitable given the time and funding constraints of a PhD project. Finally, the force produced during assessments of hip abduction strength may have been limited due to the standing position utilised, particularly in the hip arthritis group, where some

participants struggled to stand on one limb to perform this test. While standing has been considered the most physiological (Farrell and Richards 1986) and functional (Cahalan et al. 1989) position for hip abduction assessment, utilising a side-lying or supine assessment may have yielded different findings.

4.8 Chapter summary

To effectively prescribe NMES, and other rehabilitation interventions, it is crucial to understand the underlying muscle impairment in individuals with hip osteoarthritis. This study demonstrated that in addition to bilateral deficits in maximal strength of the hip abductors, knee extensors and knee flexors, hip osteoarthritis may be characterised by markedly lower muscular endurance of the knee extensors and impaired functional performance. To date, the majority of NMES interventions prescribed in lower limb populations have been prescribed to improve maximal strength measures, and therefore, further research is required to understand whether muscle endurance can be improved through NMES. The endurance capacity of the knee extensors can play an important role in daily function, and therefore the NMES intervention described in Chapter 8 was underpinned by endurance training principles.

Chapter 5. Lab-based feasibility and acceptability of NMES in hip osteoarthritis rehabilitation

5.1 Chapter introduction

The early stages of this research sought to learn more about how individuals with hip osteoarthritis would respond to NMES, to contribute towards the second objective of this thesis, which was to learn whether NMES is an acceptable and tolerable treatment modality for individuals with hip osteoarthritis. Therefore, the participants recruited in the study described in Chapter 4 were also invited to complete a lab based NMES session, where measures of feasibility and acceptability related to NMES were assessed. This chapter describes the rationale, methodology, findings, and implications from this study, and includes a published research article that comprises section 5.4 (Burgess et al. 2021b).

5.2 Rationale

While it is largely agreed that NMES is a successful method to improve muscle strength, voluntary activation and functional recovery, it remains a clinically underutilised modality in orthopaedic practice, with only limited published evidence of its use amongst people with hip osteoarthritis (Spector et al. 2016; Burgess et al. 2019). This slow transition of NMES into clinical practice has been attributed to a lack of guidelines on stimulation parameters, uncertainty regarding the feasibility of stimulation for inducing strength gains, and concerns of intolerance in patients particularly sensitive to electrical stimulation (Spector et al. 2016; Nussbaum et al. 2017). A key component of assessing the feasibility of clinical interventions is patient acceptability, which relates to how the intended recipients react to the intervention (Bowen et al. 2009). Therefore, this study was designed to investigate patient-related factors that may influence the feasibility and acceptability of using NMES as a treatment modality to counteract muscle weakness amongst adults with hip osteoarthritis.

In addition, this study was designed to compare stimulation responses of the hip abductors and knee extensors, to build on the findings from Chapter 4, and decide a muscle group to target when designing an NMES intervention. The basic theoretical premise of electrical muscle stimulation is that if the peripheral nerve can be stimulated, the resulting excitation impulse will be transmitted along the nerve to the motor endplates in the muscle, producing a muscle contraction, which can influence muscle hypertrophy, strength, and endurance, if the correct stimulation parameters are chosen. However, it is possible that not all individuals will be able to tolerate NMES at the required intensity due to pain or discomfort. Therefore, this study aimed to understand whether individuals with hip osteoarthritis could tolerate NMES of the knee extensors and hip abductors at an intensity sufficient to elicit a muscular contraction. The objectives of this study are listed below:

1. To assess tolerability and acceptability of NMES of the hip abductors and knee extensors in individuals with hip osteoarthritis.
2. To assess pain and discomfort during NMES of the hip abductors and knee extensors in individuals with hip osteoarthritis.
3. To assess muscle contractile force during NMES of the hip abductors and knee extensors in individuals with hip osteoarthritis.

5.3 Methodology

The participants included in this study are the participants described in Chapter 4 and therefore the same participant documents, ethical approval and recruitment process apply to this analysis (Appendices 1, 2 and 3). The full methodology of this study is described according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement in the published article that comprises section 5.4 of this thesis (von Elm et al. 2014).

Participants were invited to take part in an NMES testing session at Bournemouth University. This session had three aims: i) to assess tolerability and acceptability of NMES, ii) to measure any pain or discomfort experienced during NMES and iii) to assess muscle contractile force during NMES of the hip abductors and knee extensors. Specifically, the study aimed to assess whether individuals with hip osteoarthritis could tolerate NMES of the knee extensors (Figure 9) and hip abductors (Figure 10) at an intensity sufficient to elicit a muscular contraction, as defined by a minimum of grade 1 on the Medical Research Council's (MRC) scale of muscle power (Medical Research Council 2020). The knee extensors and hip abductors were chosen due to their importance for activities of daily living (Grimaldi et al. 2009; Foucher et al. 2018), and susceptibility to weakness and atrophy in hip osteoarthritis (Loureiro et al. 2013; Marshall et al. 2016; Burgess et al. 2021c), as discussed further in Chapters 2 and 4. As described in Chapter 3, the majority of research into NMES in orthopaedic populations has focused on stimulation of the knee extensors, with little research into the hip abductors. Nonetheless, preliminary research has demonstrated significant weakness in individuals with hip osteoarthritis in the early stages of the disease (Loureiro et al. 2013) and following hip replacement surgery (Vogt et al. 2010). Therefore, this study sought to determine whether both the hip abductors and knee extensors could be stimulated to produce an involuntary muscle contraction, at an intensity acceptable to the participant, to inform the design of an effective NMES programme to address muscle weakness in hip osteoarthritis.

A case-control study was considered appropriate so that outcome measures could be compared between individuals with hip osteoarthritis and healthy adults, to assess any differences in response to NMES that may be attributable to hip joint pathology. NMES was applied unilaterally to the affected limb of the participants with hip osteoarthritis, and to the right limb of the control group. For participants with bilateral hip osteoarthritis, NMES was applied to the more severely affected limb.

The device was fitted by the researcher, and then subsequently operated independently by the participant, for a period of around five minutes. Participants were asked to progressively increase the intensity of stimulation to the maximum they could tolerate. Data were collected on muscle contractile force (using the MRC scale), tolerability, pain, discomfort, and acceptability. While this study collected mostly quantitative data, we sought to understand user perspectives of NMES, and therefore at the end of the testing session, participants were able to give their feedback on the device through an open-ended question on their experience of NMES. Open ended questions allow responders to provide unstructured opinions, and therefore provide a holistic and comprehensive understanding of the intervention under investigation (Allen 2017).

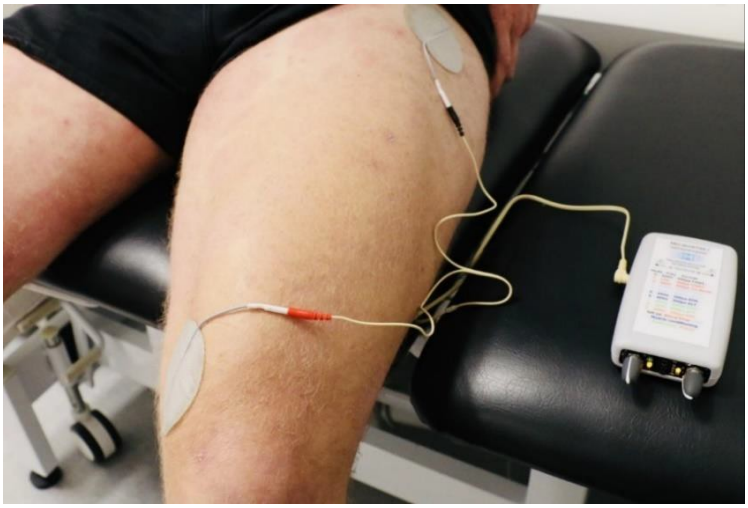


Figure 9 NMES of the knee extensors

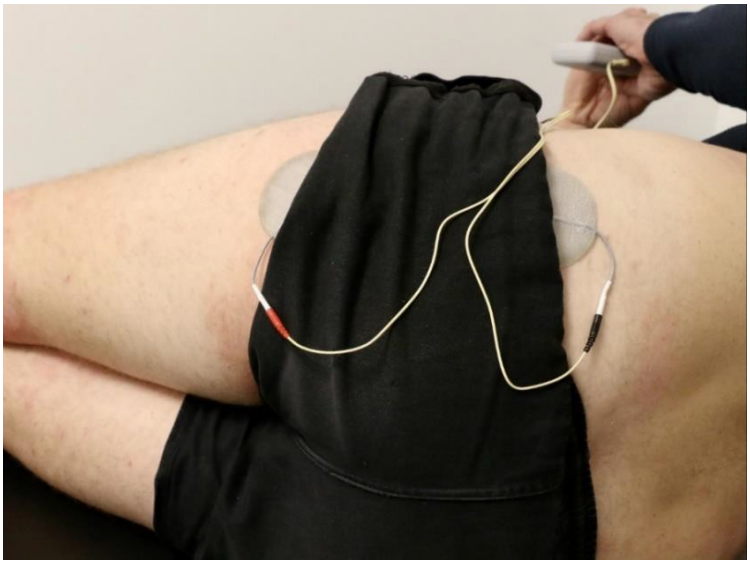


Figure 10 NMES of the hip abductors

Own images

5.4 Research article

Lab-based feasibility and acceptability of neuromuscular electrical stimulation in hip osteoarthritis rehabilitation

Louise C. Burgess, Paul Taylor, Thomas W. Wainwright & Ian D. Swain

Original Article

RATE

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Lab-based feasibility and acceptability of neuromuscular electrical stimulation in hip osteoarthritis rehabilitation

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Abstract

Introduction: Neuromuscular electrical stimulation (NMES) could provide an alternative or adjunct treatment modality to induce muscle hypertrophy in the hip osteoarthritis population. This preliminary study evaluates the feasibility and acceptability of NMES to evoke involuntary muscle contractions in adults with advanced hip osteoarthritis.

Methods: Thirteen adults with moderate-to-severe hip osteoarthritis and fifteen healthy, older adults were invited to a lab-based testing session. NMES was applied unilaterally to the knee extensors and hip abductors for one continuous, five-minute testing session. Data were collected on device acceptability, tolerability and muscle contractile force, and compared between groups.

Results: Electrical stimulation of the knee extensors elicited a visible muscular contraction in 11 participants (85%) with hip osteoarthritis and 15 controls (100%) at an intensity acceptable to the participant. Electrical stimulation of the hip abductors elicited a muscular contraction in eight participants (62%) with osteoarthritis, and ten controls (67%). Muscle contractile force, pain, discomfort and acceptability did not differ between groups, however NMES of the knee extensors was favoured across all measures of assessment when compared to the hip abductors.

Conclusions: Electrical stimulation of the knee extensors may be a feasible and acceptable treatment modality to address muscle atrophy in adults with advanced hip osteoarthritis.

Keywords

Rehabilitation devices, rehabilitation, electrical stimulation, hip osteoarthritis, NMES

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Background

Bilateral lower-limb muscle weakness and fatigue are features of individuals with advanced hip osteoarthritis,[1–6] which can lead to functional disability and an increased risk of further morbidity and mortality.[7,8] To counteract musculoskeletal impairment, local muscle strengthening and aerobic exercise are recommended irrespective of age, comorbidity, pain severity or disability.[9–12] Likewise, when progression of the disease leads to consideration for total hip replacement surgery, preoperative exercise programmes are proposed as a potential method to expedite recovery time.[13–15] Nonetheless, some patients choose to avoid traditional exercise due to fear of causing joint damage or exacerbating pain,[16–20] and the evidence supporting physiotherapy prior to hip replacement for improving function is equivocal.[13]

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Neuromuscular electrical stimulation (NMES) is an alternative treatment that can counteract muscle weakness in adults with advanced progressive diseases; and has long been used to preserve or restore skeletal muscle mass and function during and after a period of disuse due to injury, surgery, or illness.[21–23] NMES involves the application of electrical impulses to skeletal muscles, by means of surface electrodes placed over the muscle belly, with the ultimate goal to evoke visible muscular contractions.[22] The activation pattern of these contractions differs substantially from that of voluntary contractions, whereby motor units are recruited in a non-selective, spatially fixed, and temporally synchronous pattern.[24] Whilst the force contracted through muscle stimulation is not greater than that of voluntary isometric contractions, it can be used where the pathology prevents voluntary exercise at either sufficient intensity or duration to be effective, with the end goal of moving onto voluntary exercise when strength and tolerance permits.[25–27] In addition, it can be used as an adjunct modality to enhance the strengthening effects of an existing rehabilitation programme, or support patients with muscle weakness who cannot tolerate high-intensity exercise or a high-volume of low-intensity exercise.[21]

Despite the evidence supporting electrical stimulation as a method to improve muscle strength, voluntary activation and functional recovery, NMES therapy remains clinically underutilised in orthopaedic practice.[22,28,29] Moreover, whilst there has been an expansion of research in the area of knee osteoarthritis and NMES for strength improvements, investigations within hip osteoarthritis are sparse.[23,30] NMES may offer a promising alternative approach to counteract muscle inhibition and minimise atrophy and thus restore normal muscle function more effectively than voluntary exercise alone. This preliminary study aims to investigate the feasibility and patient acceptability of using NMES as a treatment option to counteract muscle weakness amongst adults with advanced hip osteoarthritis. Data are compared to healthy adults, to observe any differences in response to NMES that may be attributable to hip joint pathology.

Methods

Participants

This is an observational case-control study recruiting two study groups: i) adults with a clinical diagnosis of unilateral or bilateral hip osteoarthritis and ii) healthy adults aged over 60 years (control group) between 12th November 2019 and 15th March 2020. Participants were recruited from the local area through online advertisement and email recruitment sent to local organisations. Sixty years was chosen as the minimum age for the control group as osteoarthritis of the hip increases between the ages of 45 and 75,[31] and the average age for total hip replacement surgery is 68.0 11.4 years.[32] Participants were included in the hip osteoarthritis group if they had: i) received a clinical diagnosis of hip osteoarthritis from their general practitioner, an orthopaedic specialist or a physiotherapist; ii) presented with chronic joint pain for at least three months; iii) had an Oxford Hip score[33] of less than 40; and iv) were not on the waiting list for total hip replacement surgery. Participants were included in the control group if they were over 60 years old with no significant musculoskeletal comorbidities or neurological diseases. Exclusion criterion for both groups included: i) neurological disease affecting walking ability; ii) rheumatoid arthritis; iii) fitted with a pacemaker or other active medical implant; iv) uncontrolled epilepsy; v) sepsis or osteomyelitis; vi) known metastatic tumour involving the hip; vii) poor skin condition that prevented the use of self-adhesive electrodes; viii) not physically able to complete the testing protocol or ix) not able to provide informed consent. The experimental protocol was approved by the institutional ethics committee on 5th September 2019. In keeping with good practice, the ethical principles for medical research outlined in the Declaration of Helsinki were followed.[34] The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for the reporting of cross-sectional studies was used to guide the reporting of this study.[35]

Electrical muscle stimulation device

The NMES device chosen for this study was the Orthopaedic Microstim 2V2 neuromuscular stimulator (developed by Odstock Medical Ltd, Salisbury, UK). The device has been developed for general orthopaedic use, and for following joint replacement surgery, and consists of a stimulator box with two leads which are connected to two multiple use self-adhesive electrodes. It includes specific programmes to target muscle conditioning, endurance or power, in addition to programmes aimed at improving venous return and preventing thrombosis and pain relief modes. The programme chosen for this study was mode 0 ("set-up") which is most appropriate when first evaluating electrode positioning and stimulation intensity. Whilst it is more common for an intermittent stimulation to be delivered within clinical practice, this mode delivers a continuous stimulation output, which is useful for determining individual responses to NMES with a controlled approach. The mode delivers a frequency of 40 Hz and a pulse duration of 300ms.

Procedures

Participants were invited to attend a laboratory-based testing session. Participants were shown the NMES device and given instructions on how to operate it. The device was fitted by a researcher to the knee extensors and hip abductors of the participants. These muscle groups were chosen due to their importance for activities of daily living,[36–38] and susceptibility to weakness and atrophy in hip osteoarthritis.[1,2,39] NMES was applied unilaterally, to the affected limb of the participants with hip osteoarthritis, and to the right limb of the control group. For participants with bilateral hip osteoarthritis, NMES was applied to the more severely affected limb. To stimulate the knee extensors (the quadriceps femoris muscle group), two PALS platinum 70 mm (2.75") round electrodes were positioned on the vastus lateralis and vastus medialis, in line with manufacturer instructions (Figure 1). For the hip abductors (gluteus medius, gluteus minimus and tensor faciae latae), two 70 mm round electrodes were placed over the proximal and distal components of the gluteus medius (Figure 2). Once the device was fitted, the participant operated the device independently for a period of around five minutes. Data were collected on device acceptability, tolerability and muscle contractile force and compared between groups to observe any differences in response to NMES in participants with hip osteoarthritis and healthy, age-matched controls.

Variables

Age, weight, height and medical history were recorded from all participants. Affected side(s), duration of symptoms and the use of analgesia for pain relief were recorded from the participants in the hip osteoarthritis group. The subjective severity of hip pain when weight bearing was rated using the Numeric Pain Rating (NPR) scale (range 0–10 with 0 depicting no pain and 10 representing unbearable pain) and the severity of symptoms were quantified using the Oxford Hip Score.[33]

Tolerability. Once the device was fitted, participants independently operated the device and were instructed to gradually increase the current intensity, starting at

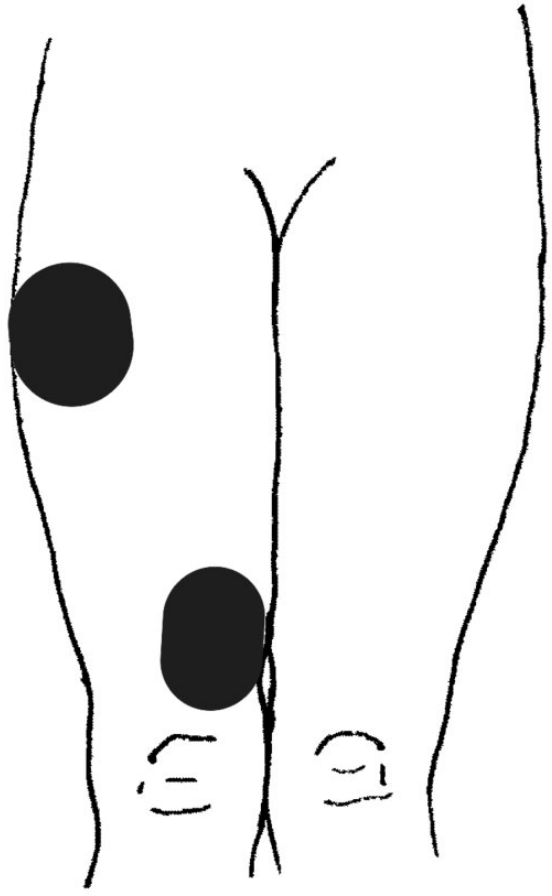

Figure 1. Electrode positioning during electrical stimulation of the knee extensors.

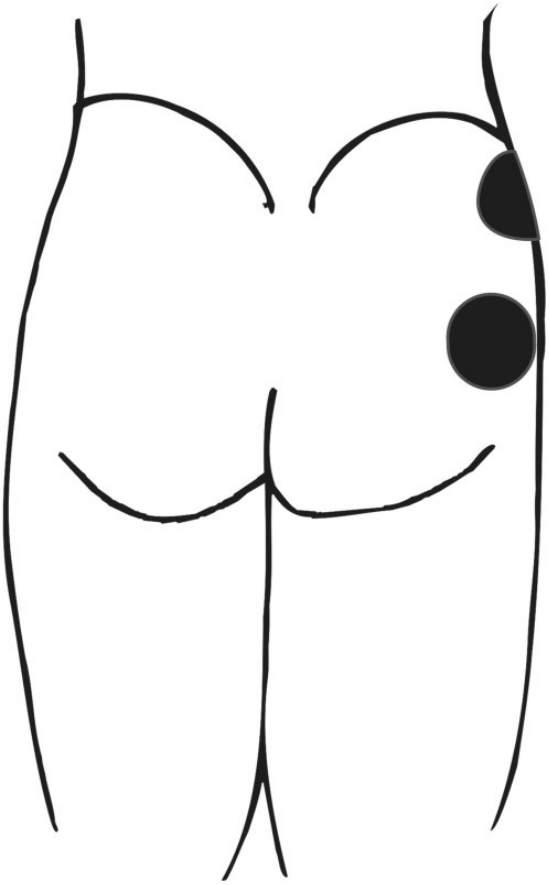

Figure 2. Electrode positioning during electrical stimulation of the hip abductors.

10 mA, until a visible involuntary muscle contraction was produced. If it was not possible to produce an involuntary muscle contraction, the participant was asked to increase the current intensity to the maximum tolerated for a period of around five minutes. Each mark on the stimulator corresponded to approximately 10 mA. The current intensity required to elicit an involuntary muscle contraction, or maximum current intensity tolerated, was recorded as a measure of device tolerability.

Pain and discomfort. Pain and discomfort were also used as measures of device tolerability. Pain during muscle contraction was recorded using a Numeric Rating Scale (NRS), with a score of zero describing no pain at all, and a score of 10 depicting the worst pain imaginable. If no visible muscle contraction was elicited, pain was recorded during the maximum stimulation intensity tolerated by the participant. Discomfort was assessed through the administration of a Likert Scale questionnaire that has previously been used to quantify discomfort associated with NMES.[40,41] Participants were asked to score their discomfort in comparison to a blood pressure cuff inflated on the arm on a scale of one to five, with a score one depicting no discomfort and a score of five describing severe discomfort.

Muscle contractile force. To evaluate if the current intensity tolerated was sufficient to evoke an involuntary muscle contraction, and the relative feasibility of the device within rehabilitation, the strength of muscle contraction produced by NMES was scored through visual inspection and the definitions used in the Medical Research Council's scale (MRC scale) of muscle power.[42] Although it does not measure strength itself, the MRC scale is the most commonly accepted method of evaluating volitional muscle activation and has proven to be reliable and accurate for clinical assessment in weak muscles.[43]

Once an involuntary muscle contraction was produced, or the participant had reached the maximum intensity of stimulation tolerable, the muscle contraction was graded independently by one researcher using the descriptions in Table 1. For example, if the NMES device could not activate a muscle contraction (no trace or flicker), the investigator would award a score of zero. If a flicker or trace of muscle activation was observed, a score of one was awarded. During knee extensor stimulation, the participant was seated on the end of a plinth, other than during the assessment of MRC grade 2. For this assessment, the participant was side lying with their leg supported. For hip abduction, the participant was side lying, with their test side up.

Table 1. MRC scale of muscle power, used with permission of the Medical Research Council.

Score	Description
0	No muscle activation
1	Trace muscle activation, such as a twitch, without achieving full range of motion
2	Muscle activation without gravity resistance, achieving full range of motion
3	Muscle activation against gravity, full range of motion
4	Muscle activation against some resistance, full range of motion
5	Muscle activation against examiner's full resistance, full range of motion

Acceptability. At the end of the testing session, participants were asked if they would consider using the device in a treatment routine (yes/no answer), and to provide any other comments or opinions about the NMES device.

Sample size and statistical methods

A formal sample size calculation was not considered appropriate given the study design.[44] Following recommendations for the design of usability studies in medical devices,[45] a sample size of 15 participants per group was sought. Data were compared between groups to observe any differences in response to NMES that may be a result of hip joint pathology.

All data were analysed using IBM SPSS Statistics version 26 (SPSS Inc., Chicago, USA), with the significance level set at $p < 0.05$. Normality of the numerical data were analysed using a Shapiro-Wilk test. If both samples passed the preliminary normality test, an independent samples t test was conducted.[46] The current intensity data were not normally distributed, and hence, a Mann-Whitney U test was conducted to compare tolerability between groups. Mean (standard deviation) and median (interquartile range (IQR)) were used to describe normally and non-normally distributed data, respectively.[47] Categorical data were analysed using a Fisher's exact test (two variables) or a Pearson's chi-squared (more than two variables) and results were presented as percentages. Participant feedback on acceptability was categorised into key themes and reported using a descriptive analysis.

Results

Fifty-eight individuals volunteered to take part in the study (Figure 3). During the initial telephone consultation, 16 volunteers did not meet the inclusion criteria due to: musculoskeletal comorbidity (n ¼ 6); prior joint

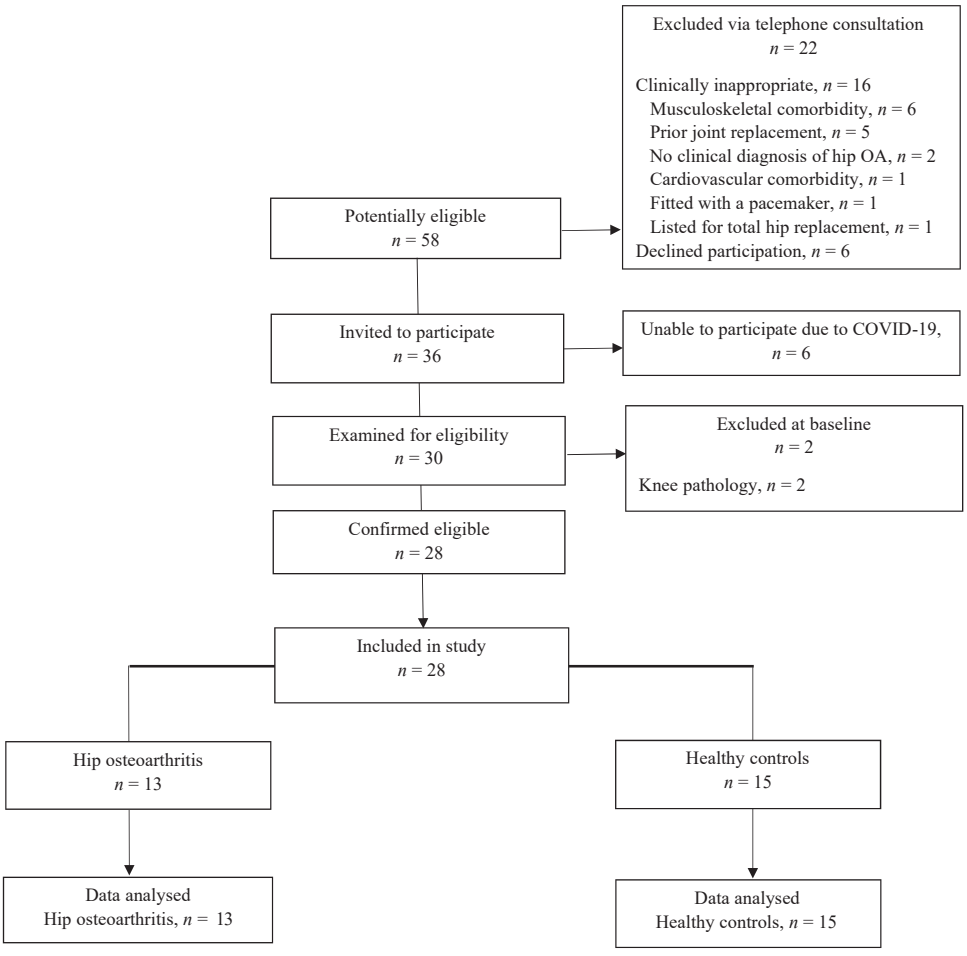

Figure 3. Participant recruitment through the study.

replacement (*n* ¼ 5); hip pain but no clinical diagnosis of osteoarthritis (*n* ¼ 2); cardiovascular comorbidity (*n* ¼ 1), fitted with a pacemaker (*n* ¼ 1); and listed for total hip replacement surgery (*n* ¼ 1), and were excluded from the study. Six participants declined participation due to travel or time commitments. A total of 36 were invited to attend the testing session. Two participants in the control group were excluded during the eligibility assessment due to knee pathology not previously disclosed. A further six participants were unable to attend the testing session due to the COVID-19 pandemic and the Government advice to close higher education institutes. Hence, the study was prematurely closed on 15th March 2020. This analysis includes 28 participants who were recruited prior to the pandemic (hip osteoarthritis, *n* ¼ 13; control group, *n* ¼ 15).

There were no differences between groups in terms of age (p ¼ 0.39) or gender distribution (p ¼ 1.00). The hip osteoarthritis group had a significantly higher BMI than the control group (p ¼ 0.03). Participants with hip osteoarthritis group had a mean Oxford Hip Score of 28 7.81 (range: 18–39), suggesting moderate-to-severe hip osteoarthritis.[33] The mean duration of symptoms was 4.04 3.17 years (range: 6 months–10 years) and mean VAS pain on weight bearing was 5.31 1.49 (range 3–8) (Table 2). Six participants were not taking any analgesics, four were taking paracetamol or ibuprofen when required, one was taking codeine and paracetamol, one was taking the maximum dose of paracetamol, and one participant was taking diahydrocodine in addition to cod liver oil.

Tolerability

All participants were comfortable with the NMES sensation and tolerated electrical stimulation of the knee extensors and hip abductors for the testing period. The median current intensity tolerated during knee extensor stimulation in the osteoarthritis group was 45 mA (IQR: 40–50), and 47 mA (IQR 40–50) in the control group. The median current intensity tolerated during

Table 2. Characteristics of participants.

Characteristic	Unilateral hip OA $n = 11$	Bilateral hip OA $n = 2$	All hip OA $n = 13$	Control group $n = 15$
Age (years)	75 7.69	72 4.95	75 7.30	72 6.42
Males, n (%)	4 (36%)	1 (50%)	5 (38%)	5 (33%)
Height (m)	1.68 0.08	1.70 9.90	1.68 0.08	1.68 0.12
Weight (kg)	83.0 18.29	91.00 4.24	84.23 17.01	71.85 14.89
BMI (kg/m^2)	29 6	32 2	30 6	25 4
Oxford Hip Score	27 7	34 5	28 7	N/A
Pain (VAS)	5.79 1.62	5.5 0.71	5.31 1.49	N/A
Duration of symptoms (years)	3.68 2.82	6.0 5.66	4.04 3.17	N/A

Table 3. Discomfort experienced during electrical stimulation of the knee extensors and hip abductors in adults with hip osteoarthritis, compared to healthy older adults.

	Knee extensors			Hip abductors		
Discomfort	Osteoarthritis	Control	Sig (2-tailed)	Osteoarthritis	Control	Sig (2-tailed)
Minimal discomfort	13 (100%)	11 (73%)	$p = 0.13$	8 (62%)	11 (73%)	$p = 0.72$
Mild discomfort	0	3 (20%)		2 (15%)	1 (7%)	
Moderate discomfort	0	1 (7%)		3 (23%)	3 (20%)	

hip abductor stimulation in the osteoarthritis group was 45 mA (IQR: 40–50) and 40 mA (IQR: 40–50) in the control group. Self-selected maximum stimulation intensity did not differ between groups during electrical stimulation of the knee extensors ($p = 0.89$) or hip abductors ($p = 0.45$).

Pain and discomfort

Pain during electrical stimulation was reported by one participant from each group during stimulation of the knee extensors. Pain was scored as 1/10 by the participant with osteoarthritis, and 4/10 by the participant in the control group. Pain during electrical stimulation of the hip abductors was reported by four participants (31%) in the osteoarthritis group (range: 2–7), and by three participants (20%) in the control group (range: 3–7). No discomfort was reported by the osteoarthritis group during stimulation of the knee extensors. Discomfort was more commonly reported during stimulation of the hip abductors (Table 3). There were no differences in discomfort between the osteoarthritis and control group during electrical stimulation of the knee extensors ($p = 0.13$) or hip abductors ($p = 0.72$).

Muscle contractile force

Neuromuscular electrical stimulation of the knee extensors evoked an involuntary muscular contraction in 11 participants (85%) in the hip osteoarthritis group and 15 participants (100%) in the control group, at a stimulation intensity acceptable to the participant. Electrical stimulation of the hip abductors evoked an involuntary muscular contraction in eight participants (62%) in the osteoarthritis group, and ten participants (67%) in the control group. Muscle contractile force, as measured by the MRC scale for muscle power, was not significantly different between study groups during stimulation of the knee extensors ($p = 0.29$) or hip abductors ($p = 1.00$). However, muscle contractile force was greater in the knee extensors, when compared to the hip abductors, in both study groups (Table 4).

Acceptability

All participants in both study groups reported that they would consider using electrical stimulation of the knee extensors and hip abductors in a treatment routine. Two participants in the osteoarthritis group and two in the control group expressed concern with the process of independently locating the muscles and placing electrodes. Two participants in the osteoarthritis group reported pain relief during stimulation of the hip abductors. Five participants in the control group said they would not have been able to tolerate a current higher than their self-selected maximum. One participant in the control group referred to the device as distracting rather than uncomfortable, and one described it as a useful alternative or adjunct to conventional exercise.

Table 4. Muscle contractile force during unilateral electrical stimulation of the knee extensors and hip abductors in adults with hip osteoarthritis, compared to healthy older adults.

	Knee extensors			Hip abductors		
MRC grade	Osteoarthritis	Control	Sig (2-tailed)	Osteoarthritis	Control	Sig (2-tailed)
0 No muscle activation	2 (15%)	0	$p = 0.29$	5 (39%)	5 (33%)	$p = 1.00$
1 Trace muscle activation	1 (8%)	4 (27%)		8 (62%)	10 (67%)	
2 Activation without gravity resistance	9 (69%)	10 (67%)		0	0	
3 Activation against gravity	1 (8%)	1 (7%)		0	0	

Discussion

Electrical muscle stimulation has a long-established place in therapy practice[48] and has been shown to preserve or restore muscle mass and aspects of neuromuscular function in a range of musculoskeletal conditions, including both acute injuries and chronic conditions.[23] Nonetheless, NMES therapy remains clinically underutilised in the hip osteoarthritis population.[30] The slow transition of NMES into clinical practice has been attributed to a lack of guidelines on stimulation parameters, uncertainty regarding the feasibility of stimulation for inducing strength gains, and concerns of intolerance in patients particularly sensitive to electrical stimulation.[22] A key component of assessing the feasibility of clinical interventions is patient acceptability, which relates to how the intended recipients react to the intervention.[49] In this preliminary study, the feasibility and acceptability of the NMES device were measured in a cohort of participants with advanced hip osteoarthritis, and compared to a cohort of healthy, age-matched controls, to observe any differences in stimulation response attributable to hip joint pathology.

Neuromuscular electrical stimulation of the knee extensors elicited a visible muscular contraction in 11 participants (85%) in the hip osteoarthritis group and 15 participants (100%) in the control group, at a stimulation intensity acceptable to the participant. Electrical stimulation of the hip abductors elicited a muscular contraction in eight participants (62%) in the osteoarthritis group, and ten participants (67%) in the control group. Muscle contractile force, pain, discomfort and acceptability did not differ between groups, however electrical stimulation of the knee extensors was favoured across all measures of assessment when compared to the hip abductors in both groups. These findings suggest that electrical stimulation of the knee extensors may be an efficacious and acceptable treatment modality to address muscle weakness in the hip osteoarthritis population. These findings are perhaps not surprising, given the evidence for NMES alone or combined with exercise for quadriceps strengthening in patients with osteoarthritis of the knee,[50] but nonetheless provide important information for future research endeavours in this area.

Importantly, no differences were observed in muscle contractile force between the two study groups during stimulation of the knee extensors or hip abductors. NMES involves the application of electrical impulses to skeletal muscles, by means of surface electrodes placed over the muscle belly, with the ultimate goal to evoke visible muscle contractions.[22] The basic theoretical premise of electrical muscle stimulation is that if the peripheral nerve can be stimulated, the resulting excitation impulse will be transmitted along the nerve to the motor endplates in the muscle, producing a muscle contraction, which will have an eventual effect on muscle hypertrophy and strength.[51] Aerobic exercise and local muscle strengthening are recommended as core components in the management of hip osteoarthritis,[9–11] however, voluntary exercise may be inhibited by pain during joint loading. During electrical stimulation of the knee extensors, it was possible to achieve muscle activation and full range of motion in the majority of participants, with only two reports of pain. Clinically, these findings are important for patients who cannot perform conventional, voluntary exercise at either sufficient intensity or duration to be effective.

Interestingly, it was not possible to achieve a muscle contraction at a tolerable level of stimulation of the hip abductors in over one third of each study group, and the most powerful contraction elicited, as graded by the MRC scale, was a trace muscle activation. These findings may be explained by a higher percentage of fatty infiltration in the gluteal muscles when compared to the quadriceps and the substantial decrease in contractile tissues of the gluteal muscles evident in patients with hip osteoarthritis.[52–55] Due to the high resistivity of subcutaneous fat tissue, higher stimulus currents are required to evoke muscle contractions where there is higher skeletal muscle fat infiltration, which can lead to patient discomfort.[56] These predictions are supported by the assessment of tolerability, whereby both pain and discomfort were more frequently

reported in both study groups during electrical stimulation of the hip abductors when compared to the knee extensors. From these findings, we can anticipate that electrical stimulation of the knee extensors will be more acceptable than electrical stimulation of the hip abductors in the hip osteoarthritis population. These findings are promising given the success of NMES applied to the knee extensors in individuals with knee osteoarthritis, whereby electrical stimulation has been shown to increase strength, train endurance, minimise atrophy, reduce pain and increase range of motion.[23,57] Future research is required to examine the effectiveness of NMES for improving knee extensor strength and endurance in the hip osteoarthritis population.

Limitations

A clear limitation of this study is the failure to meet the sample size sought due to a global pandemic and the premature completion of data collection. Participants were encouraged to answer the questions on the NMES device honestly and accurately. Nonetheless, we recognise an element of response bias may exist in the feedback of the device, whereby the participants felt they should report a favourable opinion.[58] It should be acknowledged that the size of the electrode used with electrical stimulation can markedly affect the stimulation response, and that choosing a larger electrode may have improved the strength of contraction. In addition, tolerance to stimulation can increase with repeated use,[59] and thus a higher current intensity may be achieved over time. The continuous contraction length used in this study may be less comfortable than the intermittent stimulation used most with NMES. Finally, the MRC grade is a subjective measure, and only quantifies the category of contraction strength, not strength itself.[43]

Conclusions

Neuromuscular electrical stimulation of the knee extensors may be a feasible treatment method to address muscle weakness in the hip osteoarthritis population. NMES was well-tolerated and acceptable to participants and may serve as an alternative or adjunct treatment to improve muscle function for those who have difficulty participating in voluntary exercise. Future research evaluating the effectiveness of NMES for improving strength, endurance or minimising atrophy is required to progress these findings.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: PT is a Clinical Director of Odstock Medical Limited, the company that supplied the device used in this study. PT and IS hold stocks in Odstock Medical Limited. LB and TW have no conflicting interests to declare.

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Guarantor

LB.

Contributorship

LB, IS, PT and TW conceived the study. LB, IS and PT were involved in protocol development, gaining ethical approval. LB recruited participants and analysed data. LB wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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5.5 Results synthesis

This study sought to learn more about how individuals with hip osteoarthritis would respond to NMES, and whether they were able to tolerate it at an intensity sufficient to elicit an involuntary muscular contraction. A key component of assessing the feasibility of clinical interventions is patient acceptability, and how the target population respond to the intervention (Bowen et al. 2009). To date, the majority of evidence in orthopaedic populations has targeted the knee extensors, however hip abductors demonstrate weakness in hip osteoarthritis due to a combination of muscle atrophy, reduced muscle density and muscle inhibition. This research found that NMES of the knee extensors elicited a visible muscular contraction in 11 out of 13 participants (85%) in the hip osteoarthritis and 15 out of 15 participants (100%) in the control group, at an intensity acceptable to the participant. However, NMES of the hip abductors was less successful, whereby it was possible to elicit a muscle contraction in eight participants (62%) in the osteoarthritis group, and ten participants (67%) in the control group. Muscle contractile force, pain, discomfort, and acceptability did not differ between groups, however electrical stimulation of the knee extensors was favoured across all measures of assessment when compared to the hip abductors in both groups. These findings suggest that electrical stimulation of the knee extensors may be an efficacious and acceptable treatment modality to address muscle weakness in the hip osteoarthritis population, however it may be more difficult to create strength gains by stimulation the hip abductors.

5.6 Discussion

To induce strength gains using NMES, users must be able to achieve a muscle contraction sufficient to produce hypertrophic effects and subsequent improvements to strength. The findings from this study suggest it may not be possible to stimulate the hip abductors at an intensity sufficient to induce an involuntary muscle contraction, and therefore it may be difficult to achieve strength gains with prolonged use. Several factors are critical in determining if a stimulating current is sufficient to cause neural excitation, including impedance, which is the sum of resistive, capacitive and inductive tissue components that resist the current (Benton 1981). It is possible that the higher percentage of fatty infiltration in the gluteal muscles, when compared to the quadriceps, may affect the contractile force produced by NMES (Doheny et al. 2010). Due to the high resistively of subcutaneous fat tissue, high stimulus currents are required where there is higher skeletal muscle fat infiltration, which can lead to pain or discomfort. Furthermore, it has previously been observed that persons with hip osteoarthritis may present with a decrease in contractile tissues of the gluteal muscles as a result of the disease (Rasch et al. 2007; Zacharias et al. 2016), therefore limiting the potential effects of NMES. Other factors that may have limited the effect of the stimulation are the size and orientation of the electrode, that can influence current density, and the parameters of the electrical stimulation (Benton 1981). Furthermore, participant positioning during the testing protocol may have influenced their tolerance and response to the stimulation. It had been planned to conduct further lab-based work to examine

participant response to different NMES protocols, however, limitations placed on research with human participants due to the Covid-19 pandemic meant this avenue of investigation was not pursed.

While the study described in Chapter 4 found muscle weakness in terms of MVIC to be most prominent in the hip abductors, when compared to the knee extensor and flexors, the results from this study raise questions regarding the potential effectiveness of stimulating the hip abductors. If a muscle contraction cannot be produced at an intensity tolerable to the user, it is unlikely that strength gains will occur with continuous use, as the stimulating current may not be sufficient to cause neural excitation. While the hip abductors may be the most significantly affected muscle group in terms of MVIC in individuals with hip osteoarthritis, deficits in knee extensor MVIC strength and endurance were also observed in the study described in Chapter 4. Given the significant role of the knee extensor muscle group in daily activities, and the findings from this feasibility assessment, it may be most beneficial to design an NMES intervention to target the knee extensor muscle group, as opposed to hip abductors, for individuals with hip osteoarthritis that may require treatment with hip replacement surgery.

5.7 Limitations

This study had several limitations, as described further in the published research article (section 5.4). Although participants were encouraged to answer the questions on the NMES device honestly and accurately an element of response bias may exist in the feedback of the device, whereby the participants felt they should report a favourable opinion (Smith 2014). To limit this in future studies, an independent interviewer could ask questions on the user experience of the device. It should also be acknowledged that selecting larger electrodes may have covered more motor units and thus induced a stronger muscle contraction. The continuous stimulation used in this study may be less comfortable than the intermittent stimulation used most often with NMES. In addition, this was the first time the participants had used NMES, and thus their tolerance level may improve with repeated use. The measurement of current intensity was approximate, given that each dial on the stimulator equated to approximately 10 mA. Finally, the MRC grade is a subjective measure, and only quantifies the category of contraction strength, not strength itself (Naqvi and Sherman 2020). Individual muscle forces across a joint can be estimated using surface electromyography (EMG) and may provide a more reliable measure of muscle contractile force. However, EMG driven muscle force prediction models rely on using maximal contractions to normalise EMG measurements to the highest peak amplitude recorded. Intramuscular EMG can be used to increase the sensitivity of muscle activity assessment however is a more invasive, time consuming and costly method. Therefore, given that this was a lab-based feasibility and acceptability study, description of muscle contraction strength using the MRC scale seemed most appropriate.

5.8 Chapter summary

This study sought to investigate the feasibility and acceptability of NMES to evoke involuntary muscle contractions in adults with advanced hip osteoarthritis, compared to a healthy, age-matched cohort to observe any differences in response to NMES that may be attributable to hip joint pathology. It found that NMES of the knee extensors may be a feasible treatment method to address muscle weakness in the hip osteoarthritis population. However, it is unlikely that NMES of the hip abductors can be applied at an intensity sufficient to evoke neural excitation, thereby supporting muscle hypertrophy and subsequent strength gains. NMES of the knee extensors was well-tolerated and acceptable to people with hip osteoarthritis, and their healthy counterparts, and therefore may serve as an alternative or adjunct treatment to improve muscle function for those who have difficulty participating in voluntary exercise. These findings, when combined with the findings of the strength assessment described in Chapter 4, suggest that designing an NMES programme targeted at improving the endurance capacity of the knee extensors, may be an effective rehabilitation intervention for people with hip osteoarthritis. The study described in Chapter 8 is a feasibility study, assessing the effects of an NMES intervention targeted at improving the muscle endurance of the knee extensor muscle group.

Chapter 6. The Covid-19 pandemic

6.1 Chapter introduction

Two years into this research project, the Covid-19 pandemic struck the world. This chapter summarises how the Covid-19 pandemic affected this research, and the methodological changes made due to national lockdowns, the closure of educational institutes and the suspension of joint replacement surgeries.

6.2 The timeline of Covid-19

This project was initiated in February 2018. In December 2019, the first case of severe acute respiratory syndrome coronavirus 2 that causes coronavirus disease 2019 (Covid-19) was reported (World Health Organisation (WHO) 2020). On the 11th March 2020, WHO declared the Covid-19 outbreak as a global pandemic (World Health Organisation (WHO) 2020). On the 23rd of March 2020, Prime Minster Boris Johnson announced what would become the first of three national lockdowns in England, ordering people to stay at home, with the exception of essential outings (House of Commons Library 2021). These lockdown measures legally came into force from 26th March 2020, meaning those residing in England were permitted to leave home for essential purposes only, such as buying food or medical reasons. The English government instructed the public to work from home where possible, and schools and universities alike were told to close their campuses to staff and students. The Orthopaedic Research Institute (ORI) of Bournemouth University duly closed its doors for what would be six months at first, with all staff and students instructed to work from home. Elective surgeries, such as hip and knee replacements, were cancelled to make bed space for patients with Covid-19, and all research studies were suspended or delivered remotely so staff could focus on delivering rapid trials in Covid-19. Head of ORI, Professor Robert Middleton was redeployed as a Medical Commander of Poole Hospital, to help co-ordinate responses to problems created by the pandemic (Orthopaedic Research Institute 2020b).

The summer of 2020 saw some relaxation of Covid-19 restrictions, whereby socialising was allowed in small groups observing social distancing, and the ORI team returned briefly to work from Bournemouth University campus in August 2020 (Orthopaedic Research Institute 2020a). Unfortunately, this return was short lived, as the work from home order returned on 22nd September 2020, followed by a second national lockdown on the 5th November 2020 (House of Commons Library 2021). A tiered system was trialled in December 2020, whereby restrictions on regions were set based upon their number of Covid-19 cases and hospital admissions. However, following concerns that this four-tier system was not containing the spread of the Alpha variant, national restrictions were reintroduced for the third time on the 6th of January 2021 (House of Commons Library 2021). The phased exit of the third lockdown occurred between March and July 2021, where academics

transferred from home to a hybrid model of working, and university students were allowed to return to on campus studies from 17th May 2021. Research studies were re-reviewed by university ethics committees and allowed to resume where considered safe and with appropriate Covid-19 precautions in place, such as extensive cleaning protocols and personal protective equipment.

Following the cancellation of millions of elective surgeries across the globe, hospitals cautiously resumed their surgery lists, careful not to increase the spread of Covid-19 infection amongst hospital staff and elective patients. The NHS typically carries out 330 elective hip replacements a day. This fell to an average of between one and two per day between March and April 2020 and in 2020, 58,000 fewer people than usual had their hip replaced (The Health Foundation 2021). The British Orthopaedic Association published a three-phase approach to resume surgeries in phases depending on the urgency of the surgery (British Orthopaedic Association 2020). Organisation and structural changes were explored, with the aim of addressing the considerable backlog of patients awaiting care (Gammeri et al. 2020; Wainwright 2021). ORI is currently supporting a mass clinic project, whereby an outpatient assessment clinic has been located above a local department store, to tackle the backlog of diagnostic referrals within the University Hospitals Dorset NHS Foundation Trust.

6.3 The impact of Covid-19 on research

When lockdown measures came into force in March 2020, ORI suspended all its clinical research and adapted follow ups to become remote, whereby patient reported outcome measures were collected over the telephone. Some academic staff were redeployed to the NHS to support National Institute of Health Research (NIHR) projects, and others, such as myself, were instructed to work from home and focus on desk research. The NIHR response to Covid-19 has and is continuing to have an exponential impact on the fight against Covid-19. They have funded, enabled and delivered ground-breaking research to help save lives, inform policy and provide doctors and nurses with the tools they need to prevent and treat Covid-19 (National Institute for Health Research 2022). This included developing vaccines, finding new treatments, supporting the global response to Covid, researching the long-term impact of the disease, and informing policy and decision-making.

Understandably, however, undergraduate and postgraduate research projects became difficult to complete within a university or healthcare setting during the Covid-19 era. Universities requested the suspension of student research projects during this time, and with campuses and labs closed, many PhD students were forced to create contingency plans or apply for extension grants. It became almost impossible to deliver an undergraduate or postgraduate research project within an NHS healthcare setting, or at a university where campus was closed. Furthermore, the suspension of elective joint replacement surgeries limited the patient population available to participate in such trials across both the public and private healthcare sectors. This of course had a considerable impact upon postgraduate

researchers, not just locally at Bournemouth University, but across the globe (Borgeson et al. 2021; Eigege and Kennedy 2021).

6.4 The impact of Covid-19 on research methodology

The Covid-19 pandemic created unprecedented challenges to clinical research for undergraduate and postgraduate researchers. Compared to the worldwide impact of Covid-19, millions of deaths, closure of borders, complete disruption to human life, these challenges seem only minute, however, must be noted for purpose of describing the alternative methodologies chosen when it was clear a contingency plan was required.

6.4.1 Early closure of lab-based research

The first change to note is the early closure of the lab-based projects, "Strength and endurance deficits in adults with moderate-to-severe hip osteoarthritis, compared to healthy, older adults" and "Lab-based feasibility and acceptability of NMES in hip osteoarthritis rehabilitation", described in this thesis in Chapters 4 and 5. The studies commenced on the 12th November 2019, and had planned to recruit fifteen participants with hip osteoarthritis and fifteen healthy adults to complete these studies, based upon sample size calculations of the primary outcome measure. Nonetheless, the final six participants screened for the studies were unable to attend the lab testing session due to the Government advice to close higher education institutes in March 2020. Hence, both these studies were prematurely closed on 15th March 2020, and the analyses included the 28 participants recruited prior to the pandemic. It was initially planned to re-open the study to reach the sample size target once the first lockdown was over, however as the Covid-19 era remained, and continues to remain, for longer than imagined, a decision was made to close the study with the sample size reached between November 2019 and March 2020. Despite concerns that this low sample size would affect the study results, a post-hoc power analysis suggested that it was only the knee extension MVIC outcome measure that was underpowered in the project comparing strength and endurance in adults with hip osteoarthritis to a healthy population. In the study assessing the feasibility and acceptability of NMES in adults with hip osteoarthritis, 12 participants in each group are considered acceptable for pilot and feasibility work (Julious 2005), and therefore this project remained largely unaffected by the pandemic.

6.4.2 Suspension of research involving human participants

As described in section 6.2, during the three national lockdowns, it was not possible to conduct research projects with human participants due to the campus closure of Bournemouth University. Following the first lab-based project (Chapters 4 and 5), it was planned to conduct further experimental research, comparing the effectiveness of different NMES protocols on individuals with hip osteoarthritis, to learn more about which training parameters were most effective and feasible. Unfortunately, both staff and students were not allowed to deliver non-essential research at

Bournemouth University for around 18 months. It was therefore decided to use some of this time to conduct a systematic review to investigate adherence to NMES interventions in lower limb osteoarthritis, and strategies used to increase adherence (Chapter 7). While this work was not originally planned, it was useful to inform the design of the final study in this research (Chapter 8), whereby the strategies to improve adherence were included in the study protocol.

6.4.3 Addition of narrative review in Covid-19 and NMES

Thirdly, during the first national lockdown, when research unrelated to Covid-19 had slowed and remote working was in force, I collaborated with an international group of experts to investigate the potential role of NMES to improve the recovery of critically ill Covid-19 patients admitted to the intensive care unit (ICU). To do so, a narrative review was conducted to examine the evidence, current guidelines, and proposed benefits of using NMES with this patient population (Burgess et al. 2021d). While largely unrelated to the aims and objectives of this thesis, this research project expanded my knowledge on NMES dose and application, and therefore contributed towards the study described in Chapter 8.

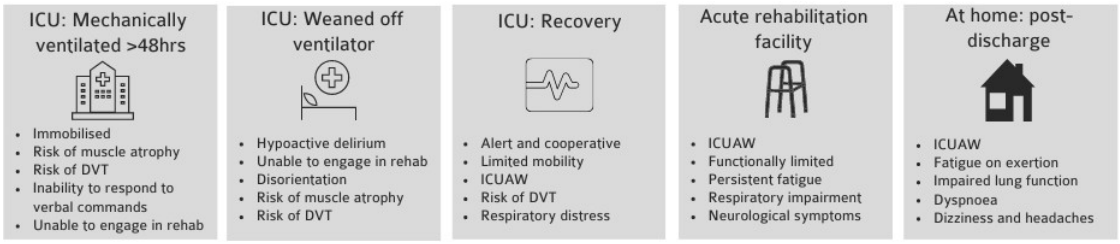

Figure 11 Stages of Covid-19 care where NMES could be applied

(Burgess et al. 2021d)

Patients with Covid-19 admitted to the ICU are often immobile and therefore at risk of muscle atrophy and venous thromboembolism yet may be unable to engage in traditional rehabilitation throughout their stay in hospital and during their recovery (Figure 11). This narrative review discusses the potential benefits of NMES to address ICU acquired weakness both in the acute and longer-term stages of recovery of individuals with Covid-19, as it can induce intermittent muscle contractions to minimize the loss of muscle mass and excitability, strengthen muscles and enhance the recovery of mobility (example application shown in Figure 12). In addition, the review discusses how NMES can be used to help wean critically ill patients off ventilators and the potential advantages of using it when a patient cannot participate in voluntary exercise. The review discusses the evidence for NMES as an alternative prophylaxis when other mechanical and pharmacological methods of prophylaxis are impractical or contraindicated, and how it could be used to manage the high rate of venous thromboembolism observed among patients with Covid-19 admitted to the ICU (example application

down in Figure 13). The narrative reviewed also offered practical and safety considerations when prescribing NMES for patients in with Covid-19, and example parameter settings (Figure 14), in hope of providing a useful guide to clinicians planning to use NMES in the ICU. The full review was published in the Journal of Rehabilitation Medicine in March 2021 (Burgess et al. 2021d).

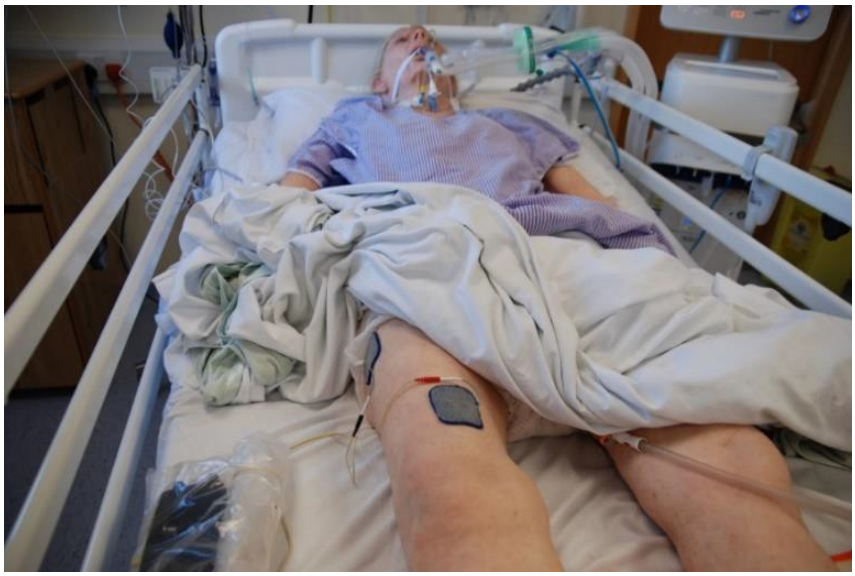

Figure 12 Electrode positioning for electrical stimulation of the quadriceps (posed with a mannequin).

Figure 13 Electrode position for electrical stimulation of the peroneal nerve for increased blood flow to the lower limb (posed with a mannequin)

(Burgess et al. 2021d)

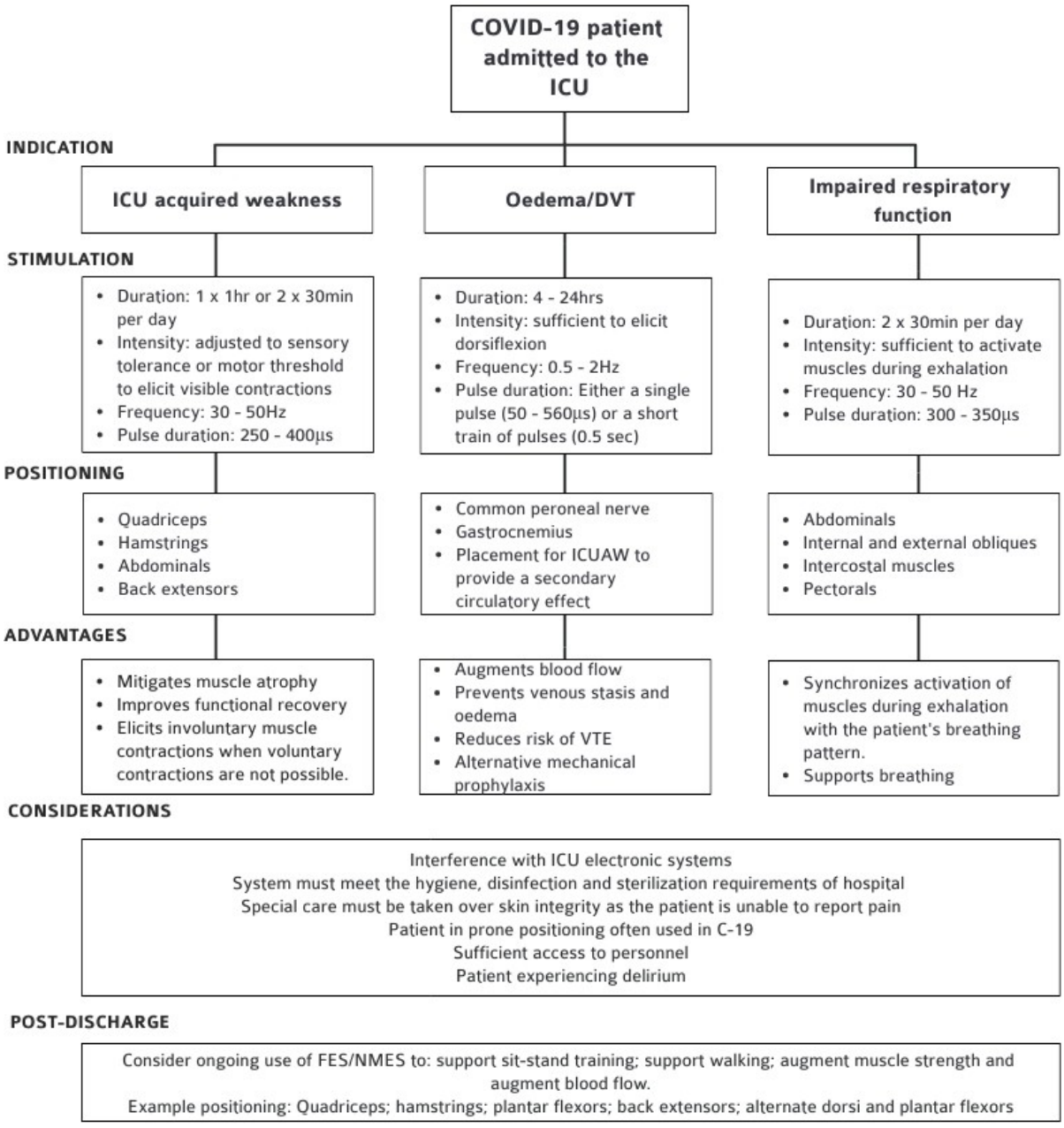

Figure 14 Example NMES settings for a patient with Covid-19 admitted to the ICU

(Burgess et al. 2021d)

6.4.4 Change in study population

Finally, when the project initiated, it was planned to test the NMES intervention amongst patients with hip osteoarthritis undergoing hip replacement surgery, to examine the feasibility of the device for improving muscle endurance and subsequent functional recovery. This research would have been novel in that few studies have analysed the effects of NMES in patients undergoing hip replacement (Burgess et al. 2019), and to date, no study had examined the potential benefits of an endurance training protocol in this population. In addition, no study has investigated NMES applied preoperatively, and how it affects postoperative recovery. The suspension of elective joint replacement surgeries, and barriers to undergraduate and postgraduate research in a healthcare setting due to Covid-19, made this study unfeasible for over two years. A second option was explored to test the NMES intervention in a non-surgical patient population with hip osteoarthritis. However, this research was also considered unfeasible due to the Covid-19 risk to a patient population. A decision was therefore made by the research team to complete the planned study protocol in healthy, older adults, as a proof-of-concept study to inform future work (Chapter 8). This can be evidenced by the amendment to the research ethics checklist, submitted to Bournemouth University's research ethics committee in Appendix 9.

6.5 Chapter summary

While the Covid-19 pandemic presented many challenges to undergraduate and postgraduate researchers, it also provided opportunities to become resilient, creative, and adaptable. Furthermore, it provided an opportunity to apply knowledge on NMES to a Covid-19 population at a time where innovations in clinical care were needed. While conducting the narrative review described in this chapter, knowledge was developed on NMES prescription and parameters, and was subsequently used to inform the design of the final study in this thesis (Chapter 8). The following two chapters describe the studies that were designed and modified in response to the ongoing Covid-19 pandemic and challenges to university and healthcare-based research.

Chapter 7. Adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis: A systematic review

7.1 Chapter introduction

In the absence of the opportunity to conduct research with human participants due to the Covid-19 pandemic, a decision was made to refer to the literature to continue progressing this research, by learning about adherence rates to NMES interventions in clinical research. While new technologies have the potential to revolutionise how health conditions are managed, and recovery from major surgery, successful implementation of new devices can only be achieved once widespread adoption has occurred. This chapter describes a systematic review that aimed to assess adherence levels to NMES interventions for muscle impairment in individuals with hip or knee osteoarthritis and compare them to adherence rates to exercise or education interventions. In addition, this review aimed to identify potential strategies to increase adherence to NMES interventions, to inform the design of the intervention described in Chapter 8. The review was published in Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders in 2021 and is included in section 7.4 of this thesis (Burgess et al. 2021a).

7.2 Rationale

Clinicians can become risk averse and resistant to change if they suspect a new technology is difficult to implement (Karsh 2004), and the driving force of recent work into NMES has been physiotherapists calling for guidance on effective parameters and application techniques required to achieve optimal results with NMES (Nussbaum et al. 2017). As NMES is a novel therapy modality within hip arthritis and hip replacement; understanding patient adherence levels and reasons for non-adherence are important factors that will affect its clinical value and widespread adoption. Moreover, increasing adherence to therapeutic programmes is recognised as an important factor for their long-term effectiveness.

The objectives of this systematic review were three-fold:

1. To quantify levels of adherence in NMES interventions for muscle impairment in hip and knee osteoarthritis
2. To identify reasons for non-adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis.
3. To identify potential strategies to increase adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis.

7.3 Methodology

This is a systematic review, registered a priori on the International Prospective Register of Systematic Reviews (PROSPERO) registration number: CRD42020224638) (Appendix 6) and reported in full in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement in section 7.4 of this thesis (Moher et al. 2015). In brief, a web-based literature search was completed in December 2020 to capture RCTs of electrical muscle stimulation in adults with hip or knee osteoarthritis. Both hip and knee studies were included, given the absence of literature in hip osteoarthritis identified in Chapter 3, however only RCTs were included so that adherence rates in NMES interventions could be compared to those in standard care, or voluntary exercise. Data were extracted from the selected manuscripts on: (i) study design; (ii) study population (sample size, type and severity of osteoarthritis); (iii) NMES dose; (iv) adherence to NMES protocol; (v) adherence in the control/comparison group; (vi) study attrition; (vii) reasons for non-adherence (as stated by the authors); (viii) potential strategies to increase adherence (as stated by the authors or considered by the researchers to be a strategy); and (ix) conclusions of the study. Mean adherence and retention rates were compared between the participants prescribed an intervention of NMES and the control/comparison group. Furthermore, mean adherence and retention rates were compared between patients who received supervised and unsupervised NMES, and between surgical and non-surgical patients. Potential strategies to increase adherence were described using a narrative synthesis and used to inform the design of the NMES intervention described in Chapter 8 of this thesis.

7.4 Research article

Adherence to Neuromuscular Electrical Stimulation Interventions for Muscle Impairment in Hip and Knee Osteoarthritis: A Systematic Review

Louise C. Burgess, Paul Taylor, Thomas W. Wainwright, Shayan Bahadori & Ian D. Swain

Adherence to Neuromuscular Electrical Stimulation Interventions for Muscle Impairment in Hip and Knee Osteoarthritis: A Systematic Review

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ABSTRACT

BACKgROuNd: Neuromuscular electrical stimulation (NMES) provides a promising approach to counteract muscle impairment in hip and knee osteoarthritis, and to expedite recovery from joint replacement surgery. Nonetheless, application into clinical orthopaedic practice remains limited, partly due to concerns regarding patient tolerance.

OBjECTIvES: This systematic review aimed to quantify levels of adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis and identify strategies to increase compliance.

dATA SOuRCES: Randomised controlled trials (RCTs) were identified in a web-based literature review, completed in December 2020. The databases sourced included the Cochrane Library, CINAHL Complete, Medline Complete and PubMed.

EligIBILITy CRITERIA: Studies were included if they were: (i) conducted in cohorts of adults with hip or knee osteoarthritis; (ii) a protocol of electrical muscle stimulation prescribed to treat muscle impairment; and (iii) reported intervention adherence or attrition rate. Data were extracted on adherence rate, reasons for non-adherence and potential strategies to increase adherence. Risk of bias was assessed using the Physiotherapy Evidence Database (PEDro) scale.

RESuLTS: The search yielded 120 articles, of which 15 studies were considered eligible and included in the analysis (n = 922). All NMES treatment was applied to the quadriceps, with 1 study targeting the quadriceps and calves. The mean PEDRO score of the included studies was 6.80 out of a possible 10 (range 6-8). Mean adherence did not differ between groups receiving treatment with NMES (85% ± 12%) and control groups receiving voluntary exercise or education (84% ± 9%) (P = .97). Reasons for non-adherence or attrition included a dislike of the device, dizziness, pain and discomfort. Strategies to increase adherence included NMES education, a familiarisation period, supervision, setting thresholds based upon patient tolerance, monitoring pain levels during stimulation and using built-in adherence trackers.

CONCLuSIONS: This systematic review indicates that adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis in clinical trials does not differ to control groups receiving education or voluntary exercise, and hence should not be a barrier to application in clinical practice.

KEywORdS: Osteoarthritis, neuromuscular electrical stimulation (NMES), joint replacement surgery, rehabilitation

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Introduction

Osteoarthritis is a chronic debilitating condition that is associated with severe pain, muscle weakness and disability.[1] In England, it is estimated that 18% of adults aged over 45 years have osteoarthritis of the knee, and 11% have osteoarthritis of the hip.[2] To counteract musculoskeletal impairment, local muscle strengthening and aerobic exercise are recommended by the National Institute of Health and Clinical Excellence (NICE), in line with international guidelines.[3-6] Likewise, when progression of the disease leads to consideration for joint replacement surgery, preoperative exercise programmes are proposed as a potential method to expedite recovery time.[7-9] Nonetheless, many patients avoid voluntary exercise due to fear of exacerbating pain or causing joint damage,[10-14] and the existing evidence regarding the value of preoperative exercise for patients undergoing joint replacement is conflicting.[7,9] Furthermore, following surgery, a decrease in voluntary muscle activation can lead to difficult and prolonged rehabilitation.[15]

Neuromuscular electrical stimulation (NMES) is a form of electrical stimulation commonly used at sufficiently high intensities to produce muscle contraction.[16] With repeated use, NMES can be used as an alternative treatment to counteract

[Title/Abstract] "hip arthri s" OR "knee arthri s" OR "hip osteoarthri s" OR "knee osteoarthri s" OR "hip replacement" OR "knee replacement" OR "hip arthroplasty" OR "knee arthroplasty" OR "joint replacement" OR "joint arthroplasty" AND [Title/Abstract] "electrical s mula on" OR "electrical muscle s mula on" OR electros mula on OR electric s mula on AND [Title/Abstract] "muscle strength" OR "muscle mass" OR strengthening OR rehabilita on OR weakness

Figure 1. Search strategy.

muscle impairment in adults with advanced progressive diseases who have difficulty activating their muscles voluntarily.[16] Therefore, NMES offers unique advantages to preserve or restore skeletal muscle mass and function during and after a period of disuse due to injury, surgery or illness, where voluntary exercise is contraindicated.[17,18] NMES involves the application of electrical impulses to skeletal muscles, by means of surface electrodes placed over the muscle belly, with the goal of evoking involuntary muscular contractions.[19] In clinical and performance sport settings, it has been proven to enhance muscle strength, increase range of motion, reduce oedema, prevent atrophy, heal tissue and decrease pain.[20] However, despite the supporting evidence; NMES remains a clinically underutilised treatment modality in the orthopaedic population.[19] In addition, in some nations, NMES is not advised in clinical guidelines for hip and knee replacement care, and is therefore only rarely used with orthopaedic patients.[21] Other reasons for limited adoption include a lack of guidelines on stimulation interventions and parameters, uncertainty regarding the efficacy of stimulation for strengthening muscles and concerns of pain in patients particularly sensitive to electrical stimulation.[19]

New technologies have the potential to revolutionise how we manage health conditions, and recovery from major surgery, both now and in the future. However, successful implementation of new devices can only be achieved once widespread adoption has occurred.[22] Clinicians can become risk averse and resistant to change if they suspect a new technology is difficult to implement.[23] The driving force of recent work into NMES has been physiotherapists calling for guidance on effective parameters and application techniques required to achieve optimal results with NMES.[24] As NMES is a novel therapy modality; understanding patient adherence levels and reasons for non-adherence are important factors that will affect its clinical value and widespread adoption. Moreover, increasing adherence to therapeutic programmes is recognised as an important factor for their long-term effectiveness. The aims of this systematic review are 3-fold: (i) to quantify levels of adherence in NMES interventions for muscle impairment in hip and knee osteoarthritis; (ii) identify reasons for non-adherence and (iii) identify potential strategies to increase adherence.

Methods

Protocol and registration

This is a systematic review, registered a priori on the International Prospective Register of Systematic Reviews (PROSPERO registration number: CRD42020224638) and reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[25] A web-based literature search was completed in December 2020 and the databases sourced included the Cochrane Library, CINAHL Complete, Medline Complete and PubMed, accessed through Bournemouth University's online library. A search strategy was developed to capture randomised controlled trials (RCTs) of electrical muscle stimulation in adults (over 18 years) diagnosed with hip or knee osteoarthritis (Figure 1). The search reviewed titles and abstracts of the available, peer-reviewed literature published from the earliest record on file until 1st December 2020. Secondary searching was also undertaken; whereby the reference lists of the yielded articles were searched for relevant citations, and to ensure the primary study was selected for inclusion.

Study selection

Selected studies were screened based on their title and abstract. Once clearly ineligible articles had been removed, full-text screening was conducted by 2 members of the research team (LB and SB). Studies were included if they were: (i) conducted in cohorts of adults with hip or knee osteoarthritis (both the non-surgical and surgical population); (ii) a protocol of electrical muscle stimulation prescribed to treat muscle impairment (NMES or NMES applied functionally, functional electrical stimulation [FES]); (iii) reported adherence (compliance to the study protocol or attrition rate); (iv) available in the English language and (v) peer-reviewed. Studies were excluded if they: (i) prescribed electrical muscle stimulation for reasons other than muscle strengthening (eg, pain relief); (ii) utilised transcutaneous electrical nerve stimulation [TENS]); (iii) prescribed NMES in combination with another strengthening modality other than standard care; (iv) did not report adherence to the electrical stimulation protocol or attrition rate; (v) were a secondary analysis or sub-group analysis of another trial or (vi) were a case-report.

Data extraction

Data were extracted from the included manuscripts into extraction sheets developed in Microsoft Excel. The following data were extracted: (i) study design; (ii) study population (sample size, type and severity of osteoarthritis); (iii) NMES dose; (iv) adherence to NMES protocol; (v) adherence in the

control/comparison group; (vi) study attrition; (vii) reasons for non-adherence (as stated by the authors); (viii) potential strategies to increase adherence (as stated by the authors or considered by the researchers to be a strategy); and (ix) conclusions of the study. If adherence rates were not reported, but the authors reported the number of participants who were non-compliant, a manual calculation was performed by dividing this number by the total number of participants in the trial arm, multiplied by 100. Retention rate was calculated by dividing the attrition rate (dropouts at all time points) by the total number of participants originally enrolled into the trial arm and multiplied by 100. To calculate mean adherence and retention rate across the included studies, each study was given an equal weighting, whereby scores were added together and divided by the number of included studies. In some studies, participants were excluded if they did not meet the target adherence for the study and therefore there is a crossover between the data extracted for study adherence and retention rate. This data is marked with an asterisk in Table 1.

Data synthesis

The characteristics of the included studies were presented using a descriptive analysis. Mean adherence and retention rates were compared between the participants prescribed an intervention of NMES and the control/comparison group. Furthermore, mean adherence and retention rates were compared between patients who received supervised and unsupervised NMES, and between surgical and non-surgical patients. The normality of this data was evaluated using a Shapiro-Wilk test. All data were normally distributed, and hence, unpaired *T*-tests were used to evaluate the relationship between groups. A Pearson's Correlation was used to investigate any relationship between duration of NMES intervention, and adherence and retention. All data were analysed using IBM SPSS Statistics version 26 (SPSS Inc., Chicago, USA), with the significance level set at $P < .05$. Correlation coefficients were interpreted using definitions from Chan.[26] Qualitative data on reasons for non-adherence and strategies to increase adherence were summarised and presented descriptively.

Quality assessment

The PEDro (Physiotherapy Evidence Database) scale was used to critically appraise the studies included within our search.[27] The methodological quality of the studies was determined independently by 2 members of the research team (LB and SB) and discrepancies were resolved through discussion with the wider research team. The 11 item scale is a valid measure used to assess clinical trials,[28,29] with each study scored out of 10; with a score of 6 as the threshold for a high-quality study (item 1 on the scale indicates external validity). The PEDro scale scores 10 items; random allocation, concealed allocation, similarity at baseline, subject blinding, therapist blinding, assessor binding, greater than 85% follow up for at least 1 key outcome, intention-to-treat analysis, between group statistical comparison for at least 1 key outcome and point and variability measures for at least 1 key outcome.[28]

Results

The search yielded 116 articles, and an additional 4 were sourced through secondary searching (Figure 2). Once duplicates (n= 16) were removed, the titles and abstracts of the remaining 104 results were screened for eligibility. Following the removal of clearly ineligible studies (n= 49), the remaining 55 studies underwent full-text screening. A further 40 studies were removed for the following reasons: did not report adherence or attrition rate (n= 13); excluded study type, or was a secondary analysis of an included study (n= 11); excluded treatment type (n= 5); excluded treatment aim (n= 4); no access to full-text (n= 3); combined treatment approach (n= 2) and not available in the English language (n= 2). Fifteen studies were considered eligible and included in the final analysis (Table 1).[30-44]

Characteristics of included studies

Fourteen of the yielded studies were randomised controlled trials[30-37,39-44] and 1 was a pilot randomised controlled trial,[38] published between 1995 and 2020.The mean PEDro score of the included studies was 6.80 out of a possible 10 (range 6-8), corresponding to a high level of internal validity (Table 2).[45] Consistently low scoring items were criterion 5 and 6, blinding of subjects and therapist. The study that compared NMES to sham stimulation was the only study that was awarded a point for item 5.[44] Other low scoring items were criterion 7 (assessor blinding) and 8 (measures of at least 1 key outcome obtained from more than 85% of the subjects initially allocated to the group).

Sample characteristics

A total of 922 participants were included in the studies, 475 of which were enrolled into an intervention of NMES that aimed to increase muscle strength or reduce atrophy. Six of the studies were conducted with patients undergoing knee replacement,[30,31,33,37,38,40] 8 were with non-surgical knee osteoarthritis patients,[32,34-36,39,42-44] and 1 study included patients listed for hip replacement surgery.[41] Treatment with the surgical arthritic population was typically postoperative, however 1 study investigated preoperative NMES, initiated 8 weeks prior to surgery,[38] and 1 study was initiated 14 days pre-surgery and continued for 60 days following surgery.[33] In the non-surgical articles, 2 studies included patients with mild-to-moderate symptoms,[32,39] 1 study included patients with moderate-to-severe symptoms,[35] 1 study included patients with end-stage osteoarthritis[44] and 4 studies included a mixed sample.[34,36,42,43]

Table 1. Summary of included studies.

STUDy AnD POPULATIOn	n	InTERvEnTIOnS	nMES DOSE	COMPARISOn InTERvEnTIOn (S)	COnCLUSIOn (S)	nMES ADHEREnCE	COMPARISOn ADHEREnCE	nMES RETEnTIOn	COMPARISOn RETEnTIOn
Klika et al[30] Knee replacement surgery	66	Postoperative, home-based, unsupervised, app controlled nMES applied to the quadriceps with a knee garment, compared to a control group (standard care).	Duration: postoperative weeks 1-12 Waveform: monophasic Frequency: 50 Hz Pulse duration: 5 ms Duty cycle 25% Current: capable of causing superior patella glide or higher as tolerated. Sessions: 3 per week Time: 20 min	Patients in both arms followed the standard of care physiotherapy regime prescribed by their surgeon, from postoperative day 1 for 12 weeks. Pain management protocols were not standardised and varied by patient and clinical practice.	Use of nMES post-operatively showed significant improvements in quadriceps strength and timed up and go scores, supporting a quicker return to function.	55%	not reported	55%*	100%
yoshida et al[31] Knee replacement surgery	77	Postoperative, supervised sensory level nMES (snMES) and motor-level nMES (mnMES) of the quadriceps, compared to a control group (standard care).	Duration: postoperative weeks 2-4 Waveform: symmetrical biphasic Frequency: 100 Hz Pulse duration: 1 ms Duty cycle: continuous/10 s on, 10 s off Current: 10-15 mA/ maximum tolerated Sessions: 5 per week Time: 45/30 min	All patients received physiotherapy from postoperative day 1 for 4 weeks, including lower extremity exercises, patellofemoral joint mobilisation and ADL exercises. 40-60 min per day, 5-6 days per week.	The mnMES group improved their muscle strength and function significantly more than standard care however reported discomfort. snMES was more comfortable and led to strength gains.	not reported	not reported	snMES = 88% mnMES = 85%	85%
Melo et al[32] Knee osteoarthritis	45	Supervised nMES training of the quadriceps compared to laser therapy (LT) and nMES combined with laser therapy (CT) in elderly women.	Duration: 8 weeks Waveform: pulsed symmetric biphasic rectangular Frequency: 80 Hz Pulse duration: 400 μs Duty cycle: not reported Current: max tolerated/40% of MvC Sessions: 2 per week Time: 18-32 min	Laser therapy applied while the probe was held stationary and perpendicular to the skin. Light pressure was applied to 3 anteromedial and 3 anterolateral points over the intercondylar notch. Two times per week, for 8 weeks.	nMES alone or combined with laser therapy increased muscle thickness and cross-sectional area.	not reported	not reported	100%	LT = 100% CT = 93%

(Continued)

Table 1. (Continued)

STUDy AnD POPULATIOn	n	InTERvEnTIOnS	nMES DOSE	COMPARISOn InTERvEnTIOn (S)	COnCLUSIOn (S)	nMES ADHEREnCE	COMPARISOn ADHEREnCE	nMES RETEnTIOn	COMPARISOn RETEnTIOn
Levine et al[33] Knee replacement surgery	70	Unsupervised pre and postoperative nMES training combined with range of motion exercises, compared to conventional, supervised physiotherapy.	Duration: 14 days pre-surgery then days 1-60 postop Waveform: not reported Frequency: not reported Pulse duration: not reported Duty cycle: not reported Current: not reported Sessions: Daily Time: not reported	Patients in the comparison group received a physiotherapy programme including progressive resistive and ROM exercises to be completed whilst hospitalised and after discharge (supervised).	Results did not differ between groups, suggesting that home-based nMES training may provide an option for simplifying and reducing the cost of postoperative physiotherapy.	not reported	not reported	80%	71%
Imoto et al[34] Knee osteoarthritis	100	Supervised quadriceps strengthening exercises and simultaneous nMES treatment compared to a control group receiving education.	Duration: 8 weeks Waveform: pulsed symmetric biphasic rectangular Frequency: 50 Hz Pulse duration: 250 μs Duty cycle: 10 s on, 30 s off Current: maximum tolerated Sessions: not reported Time: 20 min	Education was provided verbally and as a written material. The content included information on knee osteoarthritis, how to adjust ADLs and instructions on applying heat and ice packs if the patient experienced swelling or soreness.	nMES in this rehabilitation programme was effective for improving pain, function and ADLs, in comparison with a group that received education only.	90%	not reported	88%*	76%
Bruce-Band et al[35] Knee osteoarthritis	41	Unsupervised nMES training of the quadriceps compared to resistance training (RT) and a control group (CG).	Duration: 6 weeks Waveform: symmetrical biphasic square Frequency: 50 Hz Pulse duration: between 100-400 μs Duty cycle: 10 s on, 50 s off Current: maximum tolerated Sessions: 5 per week Time: 20 min	RT – 3 session per week, for 6 weeks (approx. 30 min). Patients were supplied with a logbook of lower limb exercises such as leg raises and wall squats (3 sets, 10 reps). CG – Standard care included education, weight loss, pain relief and physiotherapy.	Home-based nMES was an acceptable alternative to exercise therapy, producing similar improvements in functional capacity.	91%	RT = 83% CG = not reported	71%	RT = 71% CG = 46%

(Continued)

Table 1. (Continued)

STUDy AnD POPULATIOn	n	InTERvEnTIOnS	nMES DOSE	COMPARISOn InTERvEnTIOn (S)	COnCLUSIOn (S)	nMES ADHEREnCE	COMPARISOn ADHEREnCE	nMES RETEnTIOn	COMPARISOn RETEnTIOn
Elboim-Gabyzon et al[36] Knee osteoarthritis	63	Supervised nMES training of the quadriceps plus group exercise compared to group exercise alone.	Duration: 6 weeks Waveform: biphasic Frequency: 75 Hz Pulse duration: 200 μs Duty cycle: 10 s on, 50 s off Current: maximum tolerated Sessions: 2 per week Time: 10 contractions	Group exercise and education sessions included ROM and lower extremity muscle strengthening exercises, functional activities and balance training. 45 min sessions, conducted biweekly for 6 weeks (12 sessions).	nMES improved voluntary activation in patients with knee osteoarthritis but did not enhance its effect on muscle strength or function.	90%	79%	83%*	76%*
Stevens-Lapsley et al[37] Knee replacement surgery	66	Standard, supervised, postoperative rehabilitation combined with nMES of the quadriceps, initiated 48 h after surgery, compared to standard rehabilitation.	Duration: 6 weeks Waveform: symmetrical biphasic Frequency: 50 Hz Pulse duration: 250 μs Duty cycle: 15 s on, 45 s off Current: maximum tolerated Sessions: 2 per day, 6-7 days per week Time: 15 contractions	Standard rehabilitation included passive knee ROM, patellofemoral mobilisation, cycling, flexibility exercises, ice and heat if needed, gait training, functional and resistance training.	The early addition of nMES effectively attenuated loss of quadriceps muscle strength and improved functional performance.	77%	not reported	86%	81%
Walls et al[38] Knee replacement surgery	17	Preoperative, unsupervised, home-based nMES training of the quadriceps with a knee garment, compared to standard preoperative care.	Duration: 8 weeks Waveform: symmetrical biphasic Frequency: 50 Hz Pulse duration: between 100-400 μs Duty cycle: 5 s on, 10 s off Current: maximum tolerated Sessions: Every other day for 2 weeks, then 5 days per week. Time: 20 min	Individualised instructions on knee ROM and quadriceps strengthening exercises from a physiotherapy, for example, static quads and leg raises. Sets of 10-20 reps for each exercise, 2 × per day.	Preoperative nMES may improve quadriceps muscle strength recovery and expedite a return to normal function in patients undergoing knee replacement.	99%	not reported	82%	83%

(Continued)

Table 1. (Continued)

STUDy AnD POPULATIOn	n	InTERvEnTIOnS	nMES DOSE	COMPARISOn InTERvEnTIOn (S)	COnCLUSIOn (S)	nMES ADHEREnCE	COMPARISOn ADHEREnCE	nMES RETEnTIOn	COMPARISOn RETEnTIOn
Palmieri-Smith et al[39] Knee osteoarthritis	30	Supervised nMES training of the quadriceps delivered to women with radiographic mild to moderate osteoarthritis compared to a control group (standard care [no treatment]).	Duration: 4 weeks Waveform: alternating current Frequency: 50 Hz Pulse duration: not reported Duty cycle: 10s on, 50s off Current: maximum tolerated or at least 35% of MvC Sessions: 3 per week Time: 10 contractions	no intervention, as this is considered standard of care for those currently not seeking treatment for osteoarthritis.	Four weeks of nMES training was insufficient to induce gains in quadriceps muscle strength or activation.	88%	not reported	69%	57%
Petterson et al[40] Knee replacement patients	200	Supervised postoperative nMES training of the quadriceps and voluntary strength training, starting 2-4 weeks post-surgery, compared to an exercise group (EG) and control group who agreed to be tested 12 months post-op.	Duration: 6 weeks Waveform: sinusoidal, alternating Frequency: 50 Hz Pulse duration: not reported Duty cycle: 10 s on, 80 s off Current: max tolerated or 30% of MvC Sessions: 2-3 per week Time: 10 contractions	Both groups received outpatient physiotherapy 2-3 times per week, for 6 weeks. Interventions targeted knee extension and flexion ROM, patellar mobility, quadriceps strength, pain control and gait. 2 × 10 reps/sets progressed to 3 × 10. Weights were added to add intensity.	Progressive quadriceps strengthening with or without nMES enhances clinical improvement after knee replacement surgery, achieving similar short and long-term functional recovery.	84%	EG = 97% CG = n/A	68%	EG = 81% CG = n/A
Gremeaux et al[41] Hip replacement surgery	29	Postoperative, supervised nMES training of the quadriceps and calves combined with conventional physiotherapy in elderly patients, compared to standard care.	Duration: 5 weeks Waveform: biphasic Frequency: 10 Hz Pulse duration: 200 μs Duty cycle: 20s on, 20s off Current: maximum tolerated Sessions: 5 per week Time: 60 min	Both groups received conventional physiotherapy including exercise to increase joint ROM, muscle strength, functional status and cardiovascular conditioning. 2 h per session, 5 × per week (25 sessions).	Low-frequency stimulation improved knee extensor strength, which is one of the factors leading to greater functional independence after hip replacement.	not reported	not reported	100%	81%

(Continued)

Table 1. (Continued)

STUDy AnD POPULATIOn	n	InTERvEnTIOnS	nMES DOSE	COMPARISOn InTERvEnTIOn (S)	COnCLUSIOn (S)	nMES ADHEREnCE	COMPARISOn ADHEREnCE	nMES RETEnTIOn	COMPARISOn RETEnTIOn
Durmus et al[42] Knee osteoarthritis	50	Supervised nMES training of the quadriceps, compared to biofeedback-assisted isometric exercises, in an outpatient department.	Duration: 4 weeks Waveform: asymmetric biphasic Frequency: 50 Hz Pulse duration: 200 μs Duty cycle: 10 s on, 10 s off Current: to establish apparent muscle contraction Sessions: 5 per week Time: 20 min	Biofeedback-assisted exercise whereby patients were asked to perform isometric quadricep contractions for 10 s with 50 s relaxation. The patient was asked to increase visual and auditory signals that they perceived at every contraction.	nMES was as effective as exercise in treating knee osteoarthritis and may be considered for those who have difficulty in or contraindications to voluntary exercise.	not reported	not reported	100%	100%
Talbot et al[43] Knee osteoarthritis	38	Home-based nMES training of the quadriceps combined with education, compared to education alone.	Duration: 12 weeks Waveform: symmetrical biphasic rectangular Frequency: 50 Hz Pulse duration: 300 μs Duty cycle: 10 s on, 50 s off Current: max tolerated or progressed from 10%-40% MvC Sessions: 3 per week Time: 15 min of 15 stimulations	Arthritis self-help course, once a week for 12 weeks. The programme taught disease aetiology, self-management techniques and goal setting. Leaders were 2 nurses.	Home-based nMES in older adults with knee osteoarthritis demonstrated promising effects to knee extensor strength, chair rise ability and walk speed, without exacerbating painful symptoms.	81%	78%	90%	89%
Oldham et al[44] Knee osteoarthritis	30	A comparison of unsupervised patterned nMES, random pattern nMES, uniform stimulation and sham nMES in elderly patients on the waiting list for TKR.	Duration: 6 weeks Waveform: asymmetrical biphasic Frequency: patterned stimulation/random interpulse intervals/ uniform frequency of 8.4 Hz Pulse duration: 300 μs Duty cycle: 30 s on, 15 s off Current: minimum required to produce both visible and palpable muscle contraction Sessions: daily Time: 3 h	The sham stimulation group received stimulation comprising a single 300 μs impulse every 3 min.	no stimulation pattern emerged as being significantly better than another, although statistically significant differences between individual stimulation patterns were observed at a number of assessment weeks.	90%	not reported	Two patients dropped out, but it is not clear which group they were in.	

Abbreviations: ADL, activities of daily living; CG, control group; CT, combined therapy; EG, exercise group; LT, laser therapy; mnMES, motor-level nMES; MvC, maximal voluntary contraction; nMES, neuromuscular electrical stimulation; ROM, range of motion; RT, resistance training; snMES, sensory level nMES.
*non-compliance used as a criterion for exclusion/drop-out.

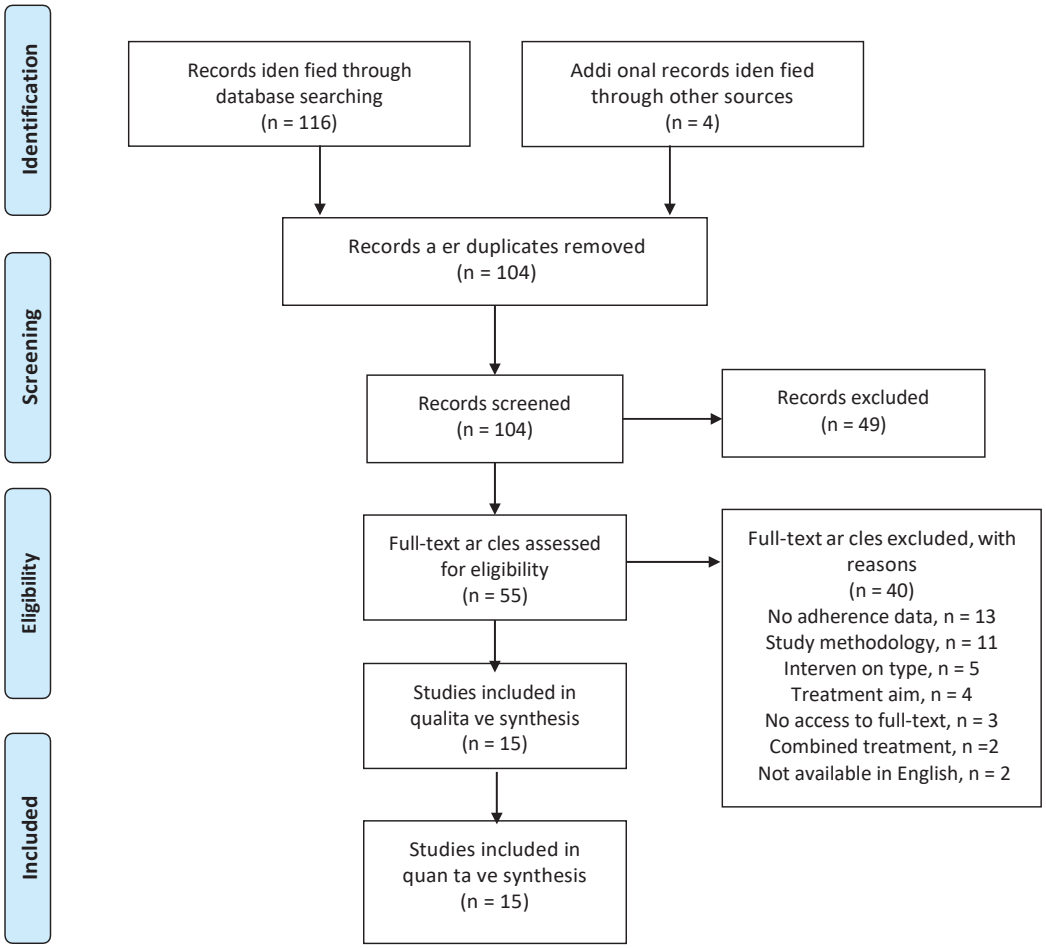

Figure 2. Study identification flowchart.[23]

Intervention characteristics

Studies were a combination of home-based, unsupervised NMES and supervised NMES, delivered in a hospital or a physiotherapy clinic. The studies compared a programme of NMES to a control group receiving no treatment,[39] conventional physiotherapy care,[30,31,33,35,37,38,40,41] voluntary exercise,[35,36,40,42] laser therapy,[32] education only[34,43] or sham stimulation.[44] Two studies compared NMES to a control group and an exercise group.[35,40] Voluntary exercise interventions included partially supervised, home-based resistance training,[35] supervised group exercise including lower-extremity strengthening, range of motion exercise, functional activities and balance training,[36] volitional strength training targeting the quadriceps at an outpatient physiotherapy department[40] and biofeedback assisted isometric contractions.[42] Standard postoperative care varied between studies, but generally included lower extremity strengthening exercise, range of motion exercises, patellofemoral mobilisation (following knee replacement only), gait training and exercises related to activities of daily living. Education groups received information on adjusting their daily living according to their symptoms,[34] and an arthritis self-help course, including details on disease aetiology, self-management techniques and goal setting.[43]

Studies ranged from 2 to 12 weeks in duration, with a median length of 6 weeks. All studies targeted the quadriceps femoris muscle group, with 1 study stimulating the quadriceps and calves.[41] Two studies investigated more than 1 type of NMES. In the study by Yoshida et al[31] sensory level NMES and motor-level NMES were compared to a control group. Oldham et al[44] compared patterned NMES, random patterned NMES and uniformed stimulation to sham NMES.

Use of NMES was reported to improve quadriceps strength,[30,31,33,38,40-44] voluntary quadriceps activation,[36] muscle thickness and cross-sectional area,[32] muscle atrophy,[37] pain[34] and functional outcome measures[30,31,33-35,37,38,42-44] however did not enhance muscle activation,[39] strength[36,39] or function[36] in 2 studies. The main conclusions from the studies are described in Table 1.

Definitions of adherence

Data on adherence were extracted from 10 studies, and data on study attrition from 14 (Table 1). For unsupervised NMES, adherence was commonly defined as the total stimulation time recorded by the device tracker or in the participant logbook, divided by the total dose prescribed and multiplied by 100. For supervised stimulation, adherence was defined as the number

Table 2. Grade of evidence PEDro score. The circle represents the study being awarded a point for each criterion of the PEDRro scale.

STUDy	n	1. ELIGIBILITy CRITERIA	2. RAnDOM ALLOCATIOn	3. COnCEALED ALLOCATIOn	4. SIMILAR GROUPS	5. SUBJECT BLInDInG	6. THERAPIST BLInDInG	7.ASSESSOR BLInDInG	8. 85% OUTCOMES	9. InTEnTIOn TO TREAT	10. OUTCOME COMPARISOn	11. vARIABILITy MEASURES	PEDRO SCORE OUTOF 10
Klika et al[30]	66	•	•	•	•			•		•	•	•	7
yoshida et al[31]	77	•	•	•	•			•	•	•	•	•	8
de Oliveira Melo et al[32]	45	•	•	•	•			•	•	•	•	•	8
Levine et al[33]	70	•	•	•	•				•	•	•	•	7
Imoto et al[34]	100	•	•	•	•			•		•	•	•	7
Bruce-Brand et al[35]	41	•	•	•	•			•		•	•	•	7
Elboim-Gabyzon et al[36]	63	•	•	•	•					•	•	•	6
Stevens-Lapsley et al[37]	66	•	•	•	•				•	•	•	•	7
Walls et al[38]	17	•	•	•	•			•		•	•	•	7
Palmieri-Smith et al[39]	30	•	•	•	•		•		•	•	•	•	8
Petterson et al[40]	200	•	•		•			•		•	•	•	6
Gremeaux et al[41]	29	•	•		•				•	•	•	•	6
Durmus et al[42]	50	•	•		•				•	•	•	•	6
Talbot et al[43]	38	•	•		•				•	•	•	•	6
Oldham et al[44]	30	•	•			•		•	•	•	•		6

of sessions attended divided by the total sessions, multiplied by 100. In 3 studies, adherence was compared between the device tracker and the participant logbook. Complete concordance was found in 2 studies[35,38] and in 1 study, the device tracker suggested a higher use than that recorded in the logbook.[43]

Adherence

Mean adherence in the NMES group was 85% ± 12% (range: 55%-99%), and 84% ± 9% (range: 78%-97%) in the comparison groups receiving exercise or education. Retention rate in the NMES group was 83% ± 13% (range: 55%-100%) and 81% ± 15% in the patients receiving standard care, laser-therapy, sham stimulation, education or voluntary exercise (range: 46%-100%). There were no differences between the NMES and comparison/control groups in terms of adherence ($P = .97$) or retention rate ($P = .64$).

Mean adherence for those receiving supervised NMES was 86% ± 6% (range: 84%-90%), and 83% ± 17% (range 55%-91%) for those receiving unsupervised NMES ($P = .76$). Mean retention rate for those receiving supervised NMES was 87% ± 12% (range 68%-100%), and 76% ± 13% (range: 55%-90%) for those receiving unsupervised NMES ($P = .16$).

Mean adherence for surgical patients was 79% ± 18% (range: 55%-99%) whereas non-surgical patients had a mean adherence rate of 88% ± 4% (range 81%-90%) ($P = .37$). Mean retention rate for surgical patients was 81% ± 14% (range: 55%-100%), and 86% ± 12% (range 69%-100%) for non-surgical patients ($P = .44$).

Pearson's correlation coefficient demonstrated a moderate, negative relationship between duration of treatment and adherence rate ($r = -.57$, $P = .08$) and a weak, negative relationship between duration of treatment and retention rate ($r = -.26$) that also did not reach significance ($P = .38$). This may be due to the small sample included within the correlation analysis.[46]

Strategies to increase adherence

Preoperative education and a familiarisation period were highlighted as potential contributors to protocol adherence.[30,37] In addition, it was speculated that supervision, or an additional home-training session to ensure safety and encourage tolerance helped to increase adherence.[34,37] In the study by Bruce-Brand et al,[35] the relative simplicity of the NMES protocol, combined with the novelty of the modality and the built-in tracker were discussed as potential reasons for high adherence. High adherence in the study by Walls et al[38] was attributed to the simplicity of garment based NMES compared to application through electrodes. However, in the study with the lowest level of adherence, NMES was also applied through a knee garment.[30]

To monitor and increase adherence the studies included: comprehensive NMES training,[35] written instructions to use devices in the home environment,[35] a clear training programme schedule,[38] an intensity threshold set to suit patient tolerance,[30] built-in adherence monitors[30,32,37,38,43,44] and participant logbooks.[33,35,37,38,43,44] In some studies, participants were aware of the built-in adherence monitor,[30,37,43,44] and in some cases, participants did not know that their adherence was being tracked.[38] Logbooks collected data on the dates and duration of the NMES sessions, amplitude settings, rate of perceived exertion and level of pain. In 1 study with surgical patients, an initial familiarisation period was used preoperatively to facilitate postoperative utilisation, and patients were required to demonstrate safe and proper use in-hospital prior to discharge.[37] In home-based interventions, some participants were visited at home to monitor an independent treatment session, to assess procedural reliability.[37,40] This was either done routinely, or in cases where concerns arose about participant implementation or tolerance to NMES. In the study by Stevens-Lapsley et al,[37] marking the electrode locations on the thigh was thought to ensure proper electrode placement, which may help increase treatment adherence and fidelity. Furthermore, an emphasis was placed on the importance of using the stimulator at an intensity that was tolerable but slightly uncomfortable.[37] To increase treatment fidelity, in 1 study, if the self-selected intensity did not result in visible contractions, the participant was excluded from the trial.[31] In the study by Gremeaux et al,[41] the degree of pain related to the stimulation was monitored every 5 sessions using a 6 level verbal scale. A score of 3 or higher resulted in exclusion from the protocol.

Reasons for non-adherence

Participants who were non-compliant reported that they did not like the device or did not want to be inconvenienced whilst recovering from surgery.[30] Other reasons for non-adherence and attrition related to the device included discomfort, dizziness and pain.[31,36,40] In the study by Stevens-Lapsley et al,[37] the authors discussed how therapists may be reluctant to push patients to tolerate uncomfortable doses of stimulation which may limit the potential benefits of the treatment. As such, the authors suggest that education regarding tolerating maximum doses of stimulation is important.[37]

Discussion

Rates of hip and knee osteoarthritis, and joint replacement surgeries, are predicted to increase in line with the ageing population and the global obesity epidemic.[47] As the National Health Service (NHS), along with health services across the globe, face rising capacity and funding challenges, the UK government has looked towards the possible benefits of new technologies to improve productivity and patient outcomes.[48] However, successful implementation of new technologies can only be achieved once widespread adoption has occurred.[22] To date, application of NMES into clinical orthopaedic practice has been slow, despite the increasing scientific evidence to support its effectiveness for treating muscle impairment.[24] Recent research has been driven by physiotherapists calling for further

guidance on effective parameters and application techniques required to achieve optimal results with NMES.[24] This review provides a synthesis of evidence for adherence to NMES interventions for muscle impairment in the hip and knee osteoarthritis population, and to our knowledge, is the first of its kind. We have identified strategies that may increase adherence when prescribing NMES and highlighted potential reasons for non-adherence. Perhaps most interestingly, we found that adherence to the prescribed treatment did not differ between groups receiving treatment with NMES and control groups receiving education or voluntary exercise. Furthermore, there were no differences in retention rates between the NMES group and patients receiving standard care, laser-therapy, sham stimulation, education or voluntary exercise. These findings are promising, given the concern that NMES may not be an acceptable treatment for patients particularly sensitive to electrical stimulation.[19]

Our findings may encourage clinicians to consider providing comprehensive NMES training, written instructions on how to use the device, a training schedule and an initial familiarisation period when prescribing NMES treatments. We also found that using patient logbooks or built-in trackers will likely encourage adherence. Adherence and retention rates amongst supervised NMES interventions were higher than unsupervised interventions, although these relationships were not significant. Likewise, non-surgical patients had higher adherence and retention rates than non-surgical patients, but these relationships were also non-significant. Potential reasons for non-adherence in NMES treatments included a dislike of the device, dizziness, pain and discomfort. Strategies to counteract these reasons could involve monitoring pain levels during stimulation and setting intensity thresholds based upon patient tolerance. However, to be effective in treating muscle impairment, stimulation intensity needs to be high enough to evoke an involuntary muscle contraction,[49] and although device trackers allow clinicians to observe total usage, it is not always possible to monitor stimulation intensity. Nonetheless, promising evidence was found in the study by Palmieri-Smith et al,[39] where stimulation intensity was evaluated during supervised treatment. Participants were able to tolerate stimulation at an intensity sufficient to achieve the target contraction strength (35% MVC or greater) in 93% of the treatment sessions.[39]

Whilst this research is novel in the area of NMES, several reviews have evaluated adherence to voluntary exercise in patients with hip and knee osteoarthritis.[50-54] One review found that just 33% of patients were fully adherent to an exercise programme prescribed following completion of the supervised element of the programme, and 37% were partially adherent.[53] Likewise, in a study by Pisters et al[55] adherence within the 3 months treatment period was reported at 57.8%, but reduced to 44.1% and 30.1% at 15 and 60 months follow up, respectively. Traditional exercise for patients chronic musculoskeletal disease can be painful, and thus adherence to voluntary exercise often reduces over time.[56] Likewise, immediately following joint replacement surgery, a decrease in voluntary muscle activation can lead to difficult and prolonged rehabilitation. Nonetheless, therapy is necessary due to significant weakness noted in the musculature in patients with lower-limb osteoarthritis and following joint replacement surgery.[15,57,58] The findings from this review suggest that adherence to NMES interventions may, in some cases, be higher than adherence to voluntary exercise interventions, and therefore provide promising results for clinicians considering treatment with NMES.

The integration of technology-based exercise programmes may have a positive effect on adherence as they can overcome perceived barriers to exercise,[59] however, must be prescribed to the right patients, in the optimal therapeutic window, with evidence-based dosing. Some patients with osteoarthritis will be contraindicated to voluntary exercise due to significant joint damage, recent joint replacement surgery or comorbidities, such as cardiac disease or hypertension.[60] Other patients may experience psychological or behavioural restrictions to voluntary exercise, such as concerns surrounding their capability to exercise, a fear of pain aggravation, along with time, transport and access restraints.[10-12] Where voluntary exercise is inhibited by pain during joint loading, NMES can be used as an alternative approach to prevent atrophy or strengthen weakened musculature. In addition, NMES offers an innovative approach to mitigate voluntary activation deficits and prevent atrophy early after surgery where a patient may be unable to generate muscle contractions of sufficient intensity to promote strength gains.[37] However, successful clinical outcomes depend upon patients' adherence to a prescribed treatment regimen,[61] and if clinicians are unsure that NMES is an acceptable treatment for patients with osteoarthritis, they may avoid prescribing it. This review found that adherence to NMES interventions for muscle impairment in hip or knee osteoarthritis does not differ to conventional physiotherapy treatments and therefore provides promising results for future clinical use. We recommend that clinicians consider the strategies identified in this review to increase adherence to NMES interventions. Future research endeavours may consider investigating optimal NMES prescription amongst orthopaedic patients, to further increase clinical adoption.

Limitations

While this review provides a summary of adherence levels to NMES interventions in research studies, estimates derived from clinical trials differ from the actual levels of adherence in the context of clinical practice, where adherence may be much lower. In addition, the analysed studies were heterogeneous, predominantly concerning patient population, sample size, comparison interventions and methods of calculating adherence. Finally, it should be considered that reasons for non-adherence and study attrition may not always be related to the

success or failure of the intervention itself. For example, some patients dropped out of the research trials due to medical necessity or family commitments.

Conclusions

Despite the supporting evidence, NMES remains a clinically underutilised treatment modality in the orthopaedic population, partly due to concerns regarding patient tolerance. This systematic review indicates that adherence to NMES interventions used to increase muscle strength or reduce atrophy in hip and knee osteoarthritis does not differ to control groups receiving education or voluntary exercise in clinical trials, and hence should not be a barrier to application in clinical practice. Reasons for non-adherence or attrition may include a dislike of the device, dizziness, pain and discomfort. Strategies to increase adherence to NMES interventions may include NMES education, a familiarisation period, setting intensity thresholds based upon patient tolerance, built-in adherence trackers, monitoring pain levels and supervision of patients during stimulation.

Author Contributions

All authors contributed to the study concept and design. LB and SB conducted the systematic review. LB, TW and IS were responsible for data extraction, analysis and interpretation. LB and SB performed the methodological quality assessment. LB drafted the manuscript. TW, IS, PT and SB reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

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7.5 Synthesis of results

This systematic review aimed to quantify levels of adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis, identify reasons for non-adherence and uncover potential strategies to increase adherence. The review found that over the duration of the study period, mean adherence in the participants receiving NMES was 85%±12% (range: 55%-99%), and 84%±9% (range: 78%-97%) in the participants receiving exercise or education interventions. Study retention rate in the NMES participants was 83%±13% (range: 55%-100%) and 81%±15% in the participants receiving standard care, laser-therapy, sham stimulation, education, or voluntary exercise (range: 46%-100%). There were no differences between the NMES and comparison/control groups in terms of adherence ($p = 0.97$) or retention rate ($p = 0.64$). In addition, no significant differences were observed in adherence rates between participants receiving supervised and unsupervised NMES, or between surgical or non-surgical participants. A correlation analysis demonstrated a moderate, negative relationship between duration of treatment and adherence rate ($r = -0.57$, $p = 0.08$) and a weak, negative relationship between duration of treatment and retention rate ($r = -0.26$) that also did not reach significance ($p = 0.38$). However, this may be due to the small sample included within the correlation analysis.

Participants who were non-compliant reported that they did not like the device or did not want to be inconvenienced whilst recovering from surgery. Other reasons for non-adherence and attrition related to the device included discomfort, dizziness, and pain. In some cases, it was not possible to determine the reason for study attrition, and therefore it is possible patients dropped out due to medical necessity, or other commitments, rather than the success or failure of the prescribed intervention. While this review focused on patient-related factors, one study included in the synthesis discussed that therapists may be reluctant to push patients to tolerate uncomfortable doses of stimulation, which may limit the potential benefits of the treatment (Stevens-Lapsley et al. 2012). Importantly, the following potential contributors to protocol adherence were discovered:

1. Comprehensive NMES training to teach the participant how to use the stimulator and where to place the electrodes.
2. A familiarisation period with a clinician/researcher.
3. Supervision during stimulation.
4. Home-based monitoring/training.
5. Monitoring pain levels during stimulation.
6. A simple and clear NMES training protocol.
7. Built in adherence trackers.
8. Participant diaries/logbooks.
9. Written instructions to use devices in the home environment.

10. Setting stimulation intensity based on patient tolerance.
11. Marking electrode placement.

7.6 Discussion

This systematic review aimed to understand whether patients adhere to NMES interventions, prescribed as part of a research study and to our knowledge, is the first of its kind. The study was designed as a response to the ongoing Covid-19 pandemic, and the inability to conduct research with human participants, and the closure of universities. Nonetheless, this study provided important findings on adherence rates, and strategies to increase adherence, that were subsequently used to inform the design of the study described in Chapter 8. In addition, this study provided important findings to answer the second objective of this thesis, which was to learn whether NMES is an acceptable and tolerable treatment modality for individuals with hip osteoarthritis.

As NMES is a novel therapy modality; understanding patient adherence levels and reasons for non-adherence are important factors that will affect its clinical value and widespread adoption. This study provided a synthesis of evidence for adherence to NMES interventions for muscle impairment in the hip and knee osteoarthritis population and identified strategies that may encourage or impede adherence when prescribing NMES. These strategies were used to encourage and monitor adherence in the final study of this thesis, described in Chapter 8, where the effectiveness of NMES for improving knee extensor endurance was assessed in a feasibility study. For example, participants received comprehensive NMES training and written instructions (Appendix 7) during their first assessment and were required to demonstrate safe and proper use of the device before starting the intervention at home. In addition, built-in adherence trackers were used to monitor adherence to the study intervention, and a participant diary (Appendix 8) was provided to encourage compliance. Participants were contacted by phone biweekly, so that NMES dose, pain and adverse events could be monitored. These strategies to increase and monitor adherence are discussed in further detail in Chapter 8.

7.7 Limitations

As discussed further in the limitations section of the published paper (section 7.4), estimates derived from clinical trials may differ from actual levels of adherence in the context of clinical practice, where adherence can be much lower. In addition, the studies included within the review were heterogenous regarding patient population, sample size, comparison intervention and methods of calculating adherence. It should be considered that reasons for non-adherence or study attrition may not always be related to the study intervention itself, or its success or failure. For example, some patients dropped out of the research trials due to medical necessity or family commitments. Future research including the perspectives of patients using NMES, and the clinicians administering stimulators, would add

further understanding regarding the barriers and facilitators to the use of NMES within clinical practice.

7.8 Chapter summary

This systematic review indicates that in clinical trials, there is no difference between adherence rates to interventions of NMES to increase muscle strength or reduce atrophy when compared to interventions of education or voluntary exercise for individuals with hip or knee osteoarthritis. Hence, concerns regarding adherence should not be a barrier to application in clinical practice. Reasons for non-adherence or attrition may include a dislike of the device, dizziness, pain, and discomfort. Strategies to increase adherence to NMES interventions may include NMES education, a familiarisation period, setting intensity thresholds based upon patient tolerance, built-in adherence trackers, monitoring pain levels and supervision of patients during stimulation. These strategies may help to improve adherence and therefore the success of NMES interventions and were incorporated into the study protocol discussed in Chapter 8 of this thesis.

Chapter 8 of this thesis has been redacted

See https://eprints.bournemouth.ac.uk/38267/

Chapter 9. Discussion

9.1 Chapter introduction

This chapter provides a discussion of the accumulated research, including a synthesis of the results in relation to the thesis aim and objectives. The main and novel findings of this research are discussed in relation to the existing evidence-base and current practice, and new and unanswered questions are highlighted. In addition, this chapter discusses the collective strengths and limitations of the research conducted, and how it can be progressed and improved in the future.

9.2 Research objectives

The broad aim of this research was to examine the feasibility of NMES for improving muscle weakness in adults with hip osteoarthritis who may require treatment with hip replacement surgery. To do this, the following objectives were formulated:

1. To gain an understanding of the physiological deficits and rehabilitation challenges common in individuals with hip osteoarthritis.
2. To learn whether NMES is an acceptable and tolerable treatment modality for individuals with hip osteoarthritis.
3. To assess the feasibility of using NMES to improve the physiological deficits and rehabilitation of individuals with hip osteoarthritis who may require treatment with hip replacement surgery.

9.3 Results summary

This research began by highlighting muscle weakness in hip osteoarthritis, the limitations of current rehabilitation practice in hip replacement surgery and the ongoing mobility issues experienced by patients in the months and years following surgery (Chapter 2). Chapter 3 introduced NMES as a potential therapy modality to overcome muscle weakness and followed with a scoping review of the available research evidence. The scoping review found i) a paucity of research exploring NMES interventions in individuals with hip osteoarthritis and ii) emerging evidence in related patient populations to support NMES for improving muscle strength and function. While the review was useful for comparing previously used methodologies, NMES interventions and outcome measures, the paucity of available evidence prevented certain conclusions being drawn regarding an optimal NMES dose, or its effectiveness in individuals with hip osteoarthritis. The review shaped the design of the subsequent experimental research, that aimed to design and test an intervention of NMES suitable for individuals with hip osteoarthritis undergoing hip replacement surgery.

The first experimental study aimed to compare lower limb maximal muscle strength and local muscular endurance in adults with hip osteoarthritis, to an age-matched control group (Burgess et al.

2021c) (Chapter 4). This study was designed to answer the first objective of this research, in combination with the literature review described in Chapters 2 and 3. To develop effective physiotherapy and exercise programmes in osteoarthritis, it is crucial to understand the underlying muscular impairment, and its relationship with physical function and disease progression. While several research efforts have addressed maximal muscular strength deficits in the hip osteoarthritis population (Loureiro et al. 2013), local muscular endurance has not been studied to the same extent, and therefore this study uncovered novel and important findings to inform subsequent research. Knee extensor muscle endurance plays an important role in functional capability during activities of daily living such as walking, rising from a chair or stair climbing (Elboim-Gabyzon et al. 2013), and has been correlated with long-term disability and mortality and cardiovascular risk factors (Vaara et al. 2014; Roshanravan et al. 2017). Given that mobility is paramount to maintaining independence in older adult and musculoskeletal populations, and the risk of cardiovascular disease in people with osteoarthritis (Wang et al. 2016a), this study informed future research investigating the role of NMES to improve knee extensor endurance.

The second experimental study involved assessing the tolerability and acceptability of NMES of the hip abductors and knee extensors in individuals with hip osteoarthritis, including measures of pain, discomfort, and muscle contractile force, to answer the second research objective (Burgess et al. 2021b) (Chapter 5). To our knowledge, this study was the first acceptability study assessing NMES tolerability in an orthopaedic population and therefore provided novel findings to inform subsequent research and the wider evidence-base. This research found that NMES of the knee extensors was tolerable and effective at producing an involuntary muscle contraction. Conversely, this study found that it was difficult to stimulate the hip abductors at an intensity sufficient to evoke a visible muscle contraction, without causing the participant pain. This was likely due to the lack of contractile tissues of the gluteal muscles, evident in individuals with hip osteoarthritis, and the amount of adipose tissues surrounding the gluteus medius, gluteus minimus and tensor fascia latae. The findings from this study were used to underpin the design of the final study (Chapter 8), that evaluated the feasibility of an NMES intervention applied to the knee extensor muscle groups.

Following this early experimental work, the Covid-19 pandemic struck. Universities closed their campuses, and clinical trials were suspended except for studies in Covid-19. In the absence of the opportunity to conduct research with human participants, a decision was made to refer to the literature to continue progressing this research, by learning about adherence rates to NMES interventions in clinical research, which further contributed to the second objective of this research. As NMES is a novel therapy modality; understanding patient adherence levels and reasons for non-adherence are important factors that will affect its clinical value and widespread adoption. Moreover, increasing adherence to therapeutic programmes is recognised as an important factor for their long-term

effectiveness. A systematic review was conducted and found that in clinical trials, there is no difference between adherence rates to interventions of NMES to increase muscle strength or reduce atrophy when compared to interventions of education or voluntary exercise for individuals with hip or knee osteoarthritis (Chapter 7) (Burgess et al. 2021a). In addition, this review uncovered important and novel information on barriers and facilitators to adherence in trials of NMES in orthopaedic populations, which were used to inform the design of the NMES intervention described in Chapter 8. This review was the first of its kind and provided a valuable synthesis of evidence for adherence to NMES intervention for muscle impairment in the hip and knee osteoarthritis population.

The aim of the final study (Chapter 8) was to answer objective 3 of the thesis, by assessing the feasibility of NMES for increasing knee extensor endurance, and subsequent functional performance, in healthy older adults, with the aim of informing future work in patients with lower limb osteoarthritis undergoing joint replacement surgery. While it had been planned to test the NMES intervention amongst arthritic patients undergoing hip replacement surgery, the suspension of elective joint replacement surgeries, and barriers to undergraduate and postgraduate research in a healthcare setting due to Covid-19, made this study unfeasible for over two years. A decision was therefore made by the research team to complete the planned study protocol in healthy, older adults, as a proof-of-concept study to inform future work. The study found that in healthy, older adults, a six-week intervention of home-based NMES applied bilaterally to the knee extensor muscle group was successful at improving bilateral muscle endurance and maximal strength. In addition, participants demonstrated bilateral improvements to their quadriceps muscle depth and thigh circumference. It is likely these muscular changes benefited participant mobility, given that improvements in functional ability were observed for all three tests (sit-to-stand, 40 m fast-paced walk and the stair negotiation test). Importantly, the measures of feasibility included in this study provided promising results for future investigations and implementation of NMES into the older adult population.

9.4 Impact of findings

9.4.1 Endurance training

The main and novel finding of this research is that knee extensor endurance and functional ability can be improved significantly in older adults though six-weeks of home-based NMES, twice a day for five days out of seven. These findings are promising given the endurance deficits observed in an older adult population with hip osteoarthritis demonstrated in Chapter 4 (Burgess et al. 2021c). Mean knee extensor endurance increased by 32% on the right leg, and median knee extensor endurance increased by 62% on the left leg. In addition, MVIC of the right leg improved by 28%, and by 32% in the left leg. These strength improvements likely improved mobility, given that sit-to-stand scores improved by 33%, walk speed by 10% and stair climb speed by 12%. To date, despite consistent supporting evidence among clinical and athlete populations, application of NMES in the orthopaedic populations

has been limited, as discussed in Chapter 3. This may be for several reasons; concerns of patient tolerance, limited resources or knowledge on application, uncertainty regarding the effectiveness of NMES or difficulty stimulating the muscles surrounding the hip, as demonstrated in Chapter 5. This research has identified an NMES intervention, targeted at improving knee extensor endurance, that will likely benefit individuals with hip osteoarthritis who require treatment with hip replacement surgery, and therefore adds important findings to the evidence-base.

Although there is a significant relationship between maximal strength and muscular endurance (McGlynn 2013), as demonstrated by the increase in endurance and maximal strength measures here, training interventions can be modified to favour adaptions in one or the other, and therefore this research provides important findings for future clinical practice. There is limited evidence available that advocates the use of NMES for overcoming sarcopenia in older adults and to date, most evidence has focused on maximal strength rather than endurance capacity (Langeard et al. 2017; Rahmati et al. 2021). Likewise, in healthy and patient populations, data of the efficacy of low-frequency NMES on muscle and functional endurance is relatively scarce (Veldman et al. 2016). Therefore, this research is novel as it describes an NMES intervention effective at improving knee extensor endurance, in addition to maximal strength. It is possible that improving maximal strength alone is not sufficient to improve skeletal muscle function in older adults. Instead, improving muscular endurance, that requires efficiency of muscle mitochondrial metabolism, may have a more significant impact on mobility (Roshanravan et al. 2017).

While maximum strength involves exerting a maximum amount of force for a short period of time, muscular endurance is the ability of the muscle or muscle group to sustain repeated contractions against a load for an extended period of time (Kell et al. 2001). Both muscle endurance and maximal strength are important for completing daily tasks, however, this study found that knee extensor endurance was more considerably impacted than maximal strength in individuals with hip osteoarthritis (Burgess et al. 2021c) (Chapter 4). In addition, in a longitudinal study of community-based older adults, knee extensor endurance was associated with a significant and linear increase in persistent lower limb limitation and mortality, whereas associations of isometric maximal torque were less certain (Roshanravan et al. 2017). Furthermore, muscular endurance has been independently associated with cardiovascular risk factors, whereas maximal strength has not (Vaara et al. 2014), suggesting advantages over endurance training rather than maximal strength training. In addition to the benefits of endurance-based NMES observed here, studies have shown that low-frequency NMES can demonstrate improvements in endurance capacity and oxygen consumption at the anaerobic threshold, possibly mediated by adaptions in aerobic-oxidative metabolism and increased capillarisation (Theriault et al. 1996; Nuhr et al. 2003; Miyamoto et al. 2016; Veldman et al. 2016). Furthermore, studies have shown that electrostimulation resistance exercise of the quadriceps muscles

can elicit a greater cardiorespiratory demand and muscle fatigue compared with voluntary contractions of the same intensity, perhaps due to the differences in patterns of motor unit recruitment between stimulated and voluntary contractions (Theurel et al. 2007).

The benefits of endurance based NMES observed here are important for several reasons. Firstly, as identified in Chapter 2, current rehabilitation practice in hip replacement surgery can be ineffective at producing a level of neuromuscular activation required to induce a muscle strength adaption (Gavin et al. 2018) and may have no effect on patient function or quality of life in the six weeks or twelve months following surgery (Smith et al. 2009). Given the improvements observed in measures of muscle strength and function here, it is likely the NMES intervention examined would be more effective at improving functional recovery than the bed exercises currently prescribed, however further studies are required to prove this. Secondly, pre and postoperative exercise interventions have been investigated for several years with the aim of improving functional recovery, and to date, no optimal rehabilitation regime has been identified (Bandholm et al. 2018). Is possible that individuals with end-stage hip osteoarthritis may not be able to tolerate the recommended dosage of strength exercise required to induce musculoskeletal benefits. On the other hand, it is possible that the exercise dose prescribed is not sufficient to evoke strengthening effects. The NMES protocol descried here offers an alternative rehabilitation strategy for the preoperative and immediate postoperative phase, where voluntary movement is limited by pain during joint loading, swelling or immobilisation. Thirdly, these findings are important as the longer duration of hip and knee osteoarthritis has been associated with an increased risk of cardiovascular disease and death (Mathieu et al. 2019; Turkiewicz et al. 2019). Therefore, given that muscular endurance has been independently associated with cardiovascular risk factors (Vaara et al. 2014), the design of an NMES intervention, suitable for individuals with hip osteoarthritis, that can improve muscular endurance is significant.

9.4.2 NMES parameters

In NMES, endurance training can be replicated by using a lower frequency, with long on times and short off times to encourage a change in muscle fibre properties from fast to slower, fatigue resistance muscle fibres, and hence increase endurance, as demonstrated in Chapter 8. To date, no study has determined optimal NMES parameters for improving endurance, and the limited, heterogenous evidence makes comparison to the success of other NMES interventions difficult. In previous studies of patients with hip osteoarthritis undergoing hip replacement, the NMES protocols involved i) one hour of stimulation a day for 12 weeks, applied to the quadriceps, at a frequency of 40 Hz, a pulse width of 250 μs and a duty cycle of 10 s on and 20 s rest (Suetta et al. 2004b; Suetta et al. 2008) and ii) one hour of stimulation for 5 days a week, for 5 weeks, applied to the quadriceps and calf muscles, at a frequency of 10 Hz, a pulse width of 200 μs and a duty cycle of 20 s on and 20 s off (Gremeaux et al. 2008). In the study by Suetta et al., NMES improved maximal gait speed by 19%, stair climbing

performance by 21% and sit-to-stand score by 21% from baseline to twelve weeks postoperatively, however had no significant effect on peak quadriceps torque or muscle size at 5 weeks or 12 weeks postoperatively. In the study by Gremeux and colleagues, the low-frequency NMES resulted in a greater improvement of knee extension on the operated side 45 days after surgery (77% vs 23%), leading to a better balance of muscle strength between the operated and non-operated limb when compared to standard physiotherapy. The NMES also led to greater improvements in Functional Independence Measure (FIM) scores but had no effect on gait speed or length of stay (Gremeaux et al. 2008).

Comparison of percentage change data from these studies to the study described in Chapter 8 is confounded, given the unique characteristics of surgical patients, and that a change from pre-surgery to post-surgery that is likely to occur regardless of the therapeutic interventions prescribed. Nonetheless, it is interesting to note the benefits of five weeks of low-frequency stimulation (10 Hz) for improving change in peak knee extensor strength (total stimulation time 25 hours), compared to the lack of effect reported by Suetta et al for 12 weeks of stimulation at 40 Hz (84 hours of stimulation). Conversely, gait speed improved in the study by Suetta et al, but not in the study by Gremeaux et al. As higher frequencies produce stronger muscle contractions, it is likely that the user will have the intensity set a lower level than they would if using a lower frequency. Therefore, these findings may be explained if the participants in the study by Suetta et al. used a lower current intensity than in the Gremeaux study. The authors suggest that perhaps the stimulation intensity was not sufficient to reach the desired level of isometric strengthening, and that the benefits to the function scores are a result of power-producing without fatigue through selective stimulation of type II muscle fibres by intermittent NMES. However, given that studies have shown that nerve recruitment is random in that electrical stimulation is as likely to excite a muscle fibre connected to a type I fibre as a type II fibre (Jubeau et al. 2007), and that motor unit recruitment during NMES likely reflects a nonselective, spatially fixed, and temporally synchronous pattern rather than in a reversal of the physiological voluntary recruitment order (Gregory and Bickel 2005), other explanations should be considered. For example, it is likely that the differences in characteristics of the study populations, or application of the NMES to the calves in the Gremeaux study could impact study outcomes.

In the study described in Chapter 8, the NMES dose included a 20 Hz frequency, with a 300 μs pulse duration, and a 10 s on and 3 s rest duty cycle, over six weeks, for a total time of 25 hours. The NMES intervention investigated in Chapter 8 observed improvements to knee extensor endurance, maximal knee extensor strength and measures of function, suggesting advantages of the dose compared to previous studies in hip osteoarthritis populations. In addition, the NMES intervention described here was successful in improving endurance measures in older adults, where previous studies have not observed improvements to fatiguability (Paillard et al. 2003; Paillard et al. 2004;

Paillard et al. 2005a; Paillard et al. 2005b; Paillard et al. 2005c). The intervention described in Chapter 8 therefore provides important findings for individuals, clinicians and exercise professionals seeking to improve lower limb muscular endurance through NMES. While these findings were accumulated as response to the ongoing rehabilitation challenges in the hip osteoarthritis population, they are relevant to other orthopaedic populations, such as individuals with knee osteoarthritis undergoing knee replacement surgery, and to the general older adult population.

9.4.3 Adherence

This research has also uncovered novel data on adherence to NMES interventions for people with lower limb osteoarthritis. The outcome of any intervention is dependent upon whether it's intended user complies with the prescribed programme, and one of the significant challenges in chronic conditions is adherence to management guidelines (Martin et al. 2005). While new technologies, such as NMES, have the potential to revolutionise how we manage health conditions, successful implementation can only be achieved once widespread adopted has occurred. Furthermore, clinicians can become risk adverse and resistant to change if they suspect a new technology is difficult to implement (Karsh 2004). The findings from the systematic review described in Chapter 7 provide promising findings that can underpin and justify the use of NMES interventions in the future. The review indicates that adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis in clinical trials does not differ to control groups receiving education or voluntary exercise, and hence should not be a barrier to application in clinical practice. In addition, this review was the first of its kind to extract strategies to increase adherence to NMES interventions and can be used to inform the design of future interventions in research and clinical practice.

Furthermore, in the feasibility study described in Chapter 8, all participants completed the study and adhered to the NMES intervention, with the mean adherence rate at 105% ± 23%, ranging from 81% - 158%, indicating that some participants were using the device for longer than prescribed. Participants reported favourable responses when asked about their experience of using the device and said they would consider using the device again. However, while this study was conducted in an age-matched cohort, studies are required to examine adherence in a clinical population, and over a longer duration of time, to determine whether adherence can be sustained. In addition, the high adherence rate observed here may in part be related to the built-in adherence tracker, as participants knew they their usage could be reviewed. Therefore, to replicate this level of adherence in clinical practice, it is possible that NMES use would need to be regularly monitored, thereby increasing therapy costs. Importantly, however, older adults were able to apply the device independently at home, with no adverse events or device deficiencies reported. Studies have shown that less than 15% of older adults regularly participate in resistance training (Merom et al. 2012), with barriers to participation including poor health, fear of risk of injury or pain, fatigue, low self-efficacy, lack of time, knowledge or

resources and a fear of risk of heart attack, stroke or death (Burton et al. 2017). Adherence may be even lower in older adults with osteoarthritis, due to severe pain and biomechanical changes to the joint that can alter their response to voluntary exercise (Latham and Liu 2010), as discussed further in Chapter 8. The findings here support the feasibility of NMES as a novel treatment modality, and indicate potential advantages over resistance training where pain, a lack of knowledge or resources, fear of risk of injury or logistical barriers may affect participation.

9.5 Recommendations for clinical application

The findings from this research suggest that it is feasible to apply an NMES intervention, targeted at improving knee extensor endurance and mobility in healthy, older adults. These findings are promising for individuals with hip osteoarthritis, who may have difficulty exercising voluntarily. The intervention described in Chapter 8 may benefit individuals undergoing hip replacement surgery, to improve their mobility and recovery post-surgery, however further research is required in a clinical population to confirm this. Application in the preoperative phase may be beneficial, where pain during joint movement limits voluntary exercise, yet muscle weakness is prominent. Furthermore application in the immediate postoperative phase, when voluntary contractions are not feasible, may help to overcome muscle atrophy due to pain, immobilisation, or swelling. Possible wider benefits, not examined in this research, may be the earlier improvement of mobility post-surgery, earlier achievement of discharge criteria, and therefore a reduced length of stay in hospital. Possible limitations of the treatment may be the time taken to train physiotherapists and patients how to usethe device, the cost of purchasing the devices and the cost of remote follow ups to monitor patient progression. Table 8 details the NMES protocol investigated in this research, and includes potential indications for use, an exclusion criteria and practical considerations, and can be used to inform the clinical application of NMES.

	Clinical application of NMES - Recommendations
Indications	Hip osteoarthritis, awaiting hip replacement. Hip osteoarthritis, post-hip replacement. Consider application to other orthopaedic populations (knee osteoarthritis, knee replacement, hip fracture). Consider application to older adults who have difficulty exercising voluntarily.
Exclusions	See list of precautions and contraindications included in NMES device manual (Odstock Medical Ltd 2020).
Electrode size	70 mm (2.75”) round electrodes Larger electrodes will likely improve strength of contraction, and smaller will likely reduce it. Larger electrodes are generally more comfortable to the user, smaller electrodes may be better for isolating muscles.
Electrode positioning	Positive: vastus medialis Negative: rectus femoris Electrode positioning is approximate and should be tested to ensure a contraction can be achieved.
User positioning	Seated, with knees slightly flexed (approximately 20° degrees flexion at knee joint).
NMES parameters	Stimulation pattern: simultaneous Frequency: 20 Hz Pulse duration: 300 μs Duty cycle: 10 s ON, 3 s OFF Ramp: 0.5 seconds Intensity: Sufficient to induce a visible muscle contraction, progressing to sufficient to induce isotonic quadriceps contraction after 2 weeks. Encourage user to increase intensity where tolerable to depolarise deeper nerve fibres. Monitor pain during increases in stimulation intensity.
Training schedule	Duration: Six weeks Days: 5 days out of 7 Week one: 2 x 15-minute sessions per day, week two: 2 x 20-minute sessions per day, week three: 2 x 25-minute sessions per day, week four: 2 x 25-minute sessions per day, week five: 2 x 30-minute sessions per day, week six: 2 x 30-minute sessions per day.
NMES training	Demonstrate NMES application on one limb of the user. The user should demonstrate safe and independent use of the device while supervised, before using it at home. Training should also be provided on precautions, safety, skin preparation, care of the device and how to rehydrate and store the electrodes.
Adherence	Utilise a built-in adherence tracker to monitor compliance and progress Utilise a participant diary to monitor discomfort, current intensity settings and usage patterns. Consider remote follow ups so NMES dose can be adjusted if necessary.
Fidelity	User should be supplied with a clear NMES training schedule, written instructions, and contact details, so they can ask questions regarding application and dose. Mark electrode placement on skin to guide user on electrode placement at home.
Practical considerations	Provide user with sufficient electrodes for treatment length. Monitor pain during stimulation. Check leads and electrodes to confirm they are conducting electricity consistently.

Table 9 Recommendations for clinical application of NMES in orthopaedic populations for strengthening purposes

9.6 Recommendations for future research

Given that the Covid-19 pandemic prevented the NMES intervention being tested in a clinical setting, future research endeavours are required to further understand the effect of NMES in an osteoarthritis population. The next stages of this research plan to test the described intervention in people awaiting hip replacement surgery, in the six weeks prior to surgery, and the six weeks following surgery to evaluate its effectiveness in improving patient mobility and recovery compared to patients receiving standard care. To add reliability and strength to this research, a blinded randomised controlled trial will be considered to prevent researcher or participant level biases (Karanicolas et al. 2010). A double-blinded trial is feasible, given that sham stimulation devices can be utilised, however participants are likely to notice that lack of muscle contraction and therefore a single-blinded trial may be more appropriate. The outcome measures chosen for the study in Chapter 8 can be utilised in this planned research, given their reliability for assessing endurance capacity, maximum strength, muscle size and functional ability. However, alternative endurance tests or hand-held dynamometry may need to be considered if outcome data is collected in a hospital setting. While partly influenced by the strength of the tester, hand-held dynamometry allows more flexibility with the location of strength testing than the dynamometer used in this research (Arnold et al. 2010). Measures related to postoperative recovery could be considered to provide data on how the use of NMES affects the achievement of discharge criteria, length of hospital stay, and quality of life. Furthermore, methods to assess the practicality of applying NMES in the immediate postoperative phase are required and should include the opinions of the healthcare practitioners applying the device and the patients operating it.

Longer term evaluations of physical activity level are required, so that the effect of NMES on activity participation can be determined. In addition, longer-term follow ups are required to understand if the endurance benefits observed here can be maintained. If not, studies are required to understand a progressive NMES dose that is effective at maintaining strength improvement to the knee extensors, without affecting usability and acceptability. Exercise is only effective for as long as it is maintained, and therefore it is important to think critically about the long-term effectiveness and sustainability of the intervention. Evaluations of costs and benefits of NMES therapy compared to current practice may also be useful to inform implementation and adoption into healthcare settings. Furthermore, comparing NMES costs to the costs associated with resistance training (for example, gym memberships, purchase of weights) may be interesting. Finally, evaluations of adherence to NMES interventions need to be conducted with longer-term follow ups, as research suggests compliance to physiotherapy interventions reduces linearly with time (Nicolson et al. 2018). This research will be useful to inform the design of strategies to increase adherence to NMES interventions in the long-term.

9.7 Unanswered questions

According to NICE, the core treatments of osteoarthritis should be education, advice and access to information, local muscle strengthening and cardiovascular exercise, and weight loss where necessary (NICE 2022). While the findings here suggest that NMES could be used as method of local muscle strengthening in the immediate pre or postoperative phase, it does not solve the problem of cardiovascular exercise or weight loss. Many individuals with hip and/or knee osteoarthritis do not meet physical activity guidance from the World Health Organisation on the volume or intensity of physical activity required to reduce the risk of mortality, heart disease, type 2 diabetes, depression, and several other diseases (Chang et al. 2020). In addition, the average BMI of patients undergoing hip replacement surgery is 28.7 (overweight) (National Joint Registry 2021), placing increased risks of complications during and after joint replacement surgery (Alvi et al. 2015). NMES training of knee extensor endurance may in part, improve endurance capacity and oxygen consumption as highlighted in this discussion. However, aerobic exercise is required to train the cardiovascular system and nutritional support may be required to support weight loss where necessary. It is possible that increases to knee extensor endurance will facilitate participation in aerobic exercise, due to improved strength, mobility and function, however further research is required to investigate this. In addition, further research is required to understand if the increased BMI in people awaiting joint replacement surgery impacts the acceptability of NMES use, as higher current intensities may be required to produce involuntary muscle contractions. Research from the Orthopaedic Research Institute continues to investigate the benefits of cycling for those with hip osteoarthritis, given its ability to provide non-weight bearing muscle strengthening and cardiovascular exercise (Wainwright et al. 2020a).

9.8 Limitations

Study design

The scoping review included in Chapter 3 was limited by the heterogenous nature of the included studies. Nonetheless, the scoping review was designed to provide a broad understanding of the current evidence-base, rather than to create certain conclusions. The experimental research was limited by the ongoing Covid-19 pandemic, closure of universities and suspension of research within healthcare settings. The planned research had sought to test an NMES intervention amongst a clinical population, whereby individuals with hip osteoarthritis receive NMES as per the protocol prescribed in Chapter 8, pre- and post-operatively. While the findings here are novel, and add to the evidence-base, evaluating whether NMES can have a clinically significant impact on people recovering from hip replacement would have yielded stronger evidence to support its use. Furthermore, comparing the intervention described here to current standard practice in a randomised controlled trial would have uncovered data that could be used to argue a change in practice. While the data presented in this thesis is useful to guide future investigations and applications of NMES, adequately powered randomised controlled

trials can be used to identify clinically meaningful changes because of an intervention, thereby increasing the likelihood they are adopted into practice.

Participants

The participants in the studies described in Chapter 4 and 5 were a population presenting with a clinical diagnosis of hip osteoarthritis, providing a reliable insight into this patient group. However, in the study described in Chapter 8, it was not possible to recruit a clinical population due to ongoing restrictions on research enforced by healthcare settings and universities alike. Given the circumstances, the participants recruited offered a reliable alternative to test the NMES intervention due to their age and gender distribution. Nonetheless, it must be highlighted that this research did not prove the effectiveness of the NMES intervention in individuals with hip osteoarthritis, but rather, the potential feasibility of it in an aged-matched healthy population. These conclusions were based upon the research conducted prior to the pandemic with a patient population, combined with the research conducted during the pandemic with a healthy, age-matched cohort. However, further clinical studies are required with a clinical population to progress this research further.

It should also be considered that the participants who took part in this research volunteered to do so, and that not all patients may be as welcome to the idea of NMES. New technologies can be difficult to implement in healthcare settings due to resistance to change, and therefore adherence and acceptability data from an unselected clinical population may differ from the values presented here. Furthermore, this research did not seek to understand the challenges and barriers that clinicians face when using NMES pre and postoperatively. Including clinicians in the design of the final study (Chapter 8) may have ensured the intervention described was truly feasible to implement in a healthcare setting.

9.9 Strengths

Study design

The quantitative nature of Chapters 4, 5, 7 and 8 add confidence to the conclusions drawn in this thesis. To integrate novel medical devices into clinical practice, quantitative approaches are needed to create scientific objectivity and justification for their use (Carr 1994; McCusker and Gunaydin 2015). Given that the majority of the data here were objective, it was possible to use statistical analyses to demonstrate the significance of the findings. In addition, this study collected a small amount of qualitative data, whereby participants were able to give their feedback on the device. Gathering participant perceptions on a proposed intervention is paramount to ensure it is truly feasible and is important to ensure future interventions are informed by the opinions of its intended user.

Data collection

A strength of this research is the outcome measures used to assess the feasibility of the NMES intervention. Dynamometry is a reliable and objective method of assessing strength and endurance, and the reliability of dynamometry for assessing knee extension and flexion has previously been proven (Sole et al. 2007). The inclusion of performance based functional assessment as per recommendations from OARSI (Dobson et al. 2013a) allow the findings here to be compared to other orthopaedic populations, and allow a true insight into participant mobility. Furthermore, the addition of ultrasonography for the final study (Chapter 8) added value due to its reliability for measuring change in skeletal muscle mass (Pillen and van Alfen 2011). While the manual circumference measurement added in the final study provided a practical and reliable estimate of leg size (Bakar et al. 2017), it is not possible to determine if increase in circumference is a result of increased muscles fibres, or fatty tissues. Therefore, the addition of thigh circumference measurements added only limited value to the study findings, however, when combined with the findings of the ultrasound measurements, were useful to understand change in muscle size because of NMES.

9.10 Chapter summary

This chapter has discussed the research conducted in relation to the existing evidence-base and current practice. In addition, it has provided recommendations for future clinical practice and research endeavours and concludes by highlighting the collective strengths and limitations of the research conducted. While the course of this research changed due to the Covid-19 pandemic, it was successful in designing a novel NMES intervention, underpinned by the physiological deficits common in individuals with hip osteoarthritis, that will likely benefit individuals with hip osteoarthritis undergoing hip replacement surgery. In addition, this research was novel due to its findings on muscle endurance deficits in individuals with hip osteoarthritis (Chapter 4), the inclusion of NMES acceptability testing (Chapter 5) and the strategies to increase adherence to NMES in orthopaedic populations uncovered in Chapter 7.

Chapter 10. Conclusions

Generally, patients recover well from hip replacement surgery, however some do not return to physical activity, work, or leisure activities (Smith et al. 2018) and therefore there are still significant rehabilitation challenges in this population (Bandholm et al. 2018). Despite this, not all hospitals offer routine, pre or post-discharge physiotherapy for joint replacement surgery. Instead, it's generally offered on a case-by-case basis, to patients with significant functional limitations or cognitive impairment (NICE 2020). In most cases, following surgery, patients will be discharged home with exercise advice in the form of a patient information leaflet and told to progress independently until their six week follow up (NICE 2020). Patient information leaflets often contain advice on recovery from surgery and exercise prescription in the form of bed exercises and sitting and standing exercises. While they can be beneficial to guide the patient through their postoperative recovery, patient information leaflets are often designed on a 'one size fits all' basis, and rarely offer advice on progressing the frequency or intensity of the exercise (Wainwright and Burgess 2018). Preliminary work has found that bed exercises are ineffective at producing a level of neuromuscular activation required to induce a muscle strength adaption (Gavin et al. 2018) and have no effect on patient function or quality of life in the six weeks or twelve months following surgery (Smith et al. 2008; Smith et al. 2009). Furthermore, while muscle strength can be improved through voluntary resistance training, studies have shown older adult and osteoarthritic populations may be reluctant to participate in voluntary resistance training due to pain, discomfort, and logistical and financial barriers (Picorelli et al. 2014; Jansons et al. 2017), and therefore innovations are required to address muscle weakness.

This research was designed to investigate the feasibility of the use of neuromuscular electrical stimulation (NMES) for addressing muscle weakness in individuals with hip osteoarthritis, who may require treatment with hip replacement surgery, in response to the ongoing rehabilitation challenges in this patient population. NMES is a treatment that can counteract muscle impairment in adults with advanced progressive diseases who have difficulty activating their muscles voluntarily (Jones et al. 2016; Nussbaum et al. 2017). However, the scoping review conducted in Chapter 3 suggests that research in this area remains limited, and it is not currently recommended by NICE in osteoarthritis due to the limited and heterogenous supporting evidence (NICE 2022). The scoping review identified a gap in the literature whereby to date, just two studies had investigated NMES in isolation for improving recovery for those with end-stage hip osteoarthritis requiring hip replacement surgery. The broad aim of this study was therefore to examine the feasibility of NMES for improving muscle weakness in adults with hip osteoarthritis who may require treatment with hip replacement surgery. This study primarily used quantitative research methods to collect, analyse and interpret data on NMES use in the target population, through a combination of descriptive, observational, and experimental research. In addition, given that a key aspect of feasibility is patient acceptability, this

study also collected qualitative data whereby participants were asked to give their feedback on the use of NMES.

This study began by identifying knee extensor muscle endurance as an important measure to improve through rehabilitation programmes, given the 70% weakness observed in the affected limb, and a 62% weakness of the contralateral limb, of individuals with hip osteoarthritis compared to an age-matched control group. While deficits in maximal isometric strength for those with hip osteoarthritis are well reported in the literature, to our knowledge, no study has examined isotonic muscle endurance in this population. While these findings are perhaps not surprising, given that muscle atrophy in osteoarthritis is homogeneous amongst both fibre types, and the relationship between maximal isometric strength and relative muscular endurance, they provided novel data to underpin the design of an NMES intervention suitable for those with hip osteoarthritis.

The design of the eventual NMES intervention was also informed by the findings of Chapter 5, whereby a lab-based acceptability study was conducted to examine measures of pain, discomfort and contractile force when applying NMES to the knee extensor and hip abductor muscles in individuals with hip osteoarthritis. To our knowledge, this study was the first acceptability study assessing NMES tolerability in an orthopaedic population and therefore provided novel findings to inform subsequent research and the wider evidence-base. This research found that NMES of the knee extensors was tolerable and effective at producing an involuntary muscle contraction. Conversely, this study found that it was difficult to stimulate the hip abductors at an intensity sufficient to evoke a visible muscle contraction, without causing the participant pain. This was likely due to the lack of contractile tissues of the gluteal muscles, evident in individuals with hip osteoarthritis, and an increase in resistive tissues surrounding the gluteus medius, gluteus minimus and tensor fascia latae.

Following this early experimental work, the course of this research changed direction slightly, given the inability to conduct research with human participants due to the Covid-19 pandemic. A systematic review was instead conducted to learn about adherence rates to NMES interventions in lower-limb osteoarthritis populations and identify strategies to increase adherence and was the first of its kind. This research was important as the outcome of any intervention is dependent upon whether it's intended user complies with the prescribed programme, and one of the significant challenges in chronic conditions is adherence to management guidelines. This review found that adherence to NMES interventions for muscle impairment in hip and knee osteoarthritis in clinical trials does not differ to control groups receiving education or voluntary exercise, and hence should not be a barrier to application in clinical practice. Importantly, the following potential contributors to protocol adherence were discovered and used to inform the design of the final study in this research:

1. Comprehensive NMES training to teach the participant how to use the stimulator and where to place the electrodes.
2. A familiarisation period with a clinician/researcher.
3. Supervision during stimulation.
4. Home-based monitoring/training.
5. Monitoring pain levels during stimulation.
6. A simple and clear NMES training protocol.
7. Built in adherence trackers.
8. Participant diaries/logbooks.
9. Written instructions to use devices in the home environment.
10. Setting stimulation intensity based on patient tolerance.
11. Marking electrode placement.

The final study in this research sought to determine the feasibility of an NMES intervention, designed in response to the preliminary research, for people with hip osteoarthritis undergoing hip replacement surgery. The study found that in healthy, older adults, a six-week intervention of home-based NMES applied bilaterally to the knee extensor muscle group was successful at improving bilateral muscle endurance and maximal isometric strength. In addition, participants demonstrated bilateral improvements to their quadriceps muscle depth and thigh circumference. It is likely these muscular changes benefited participant mobility, given that improvements to functional ability were observed for all three tests. Importantly, the measures of feasibility included in this study provided promising results for future investigations and implementation of NMES into the older adult population. These finding are significant; given the limitations of current rehabilitation practice, and the ongoing rehabilitation challenges following joint replacement surgery. Furthermore, the intervention designed adds to the evidence-base for NMES use in general older adult populations. However, due to the Covid-19 pandemic, closure of universities and restrictions on clinical research, further research is required to test the proposed intervention in a clinical population.

Recommendations for future research

Future research endeavours should involve applying the intervention described here to a clinical population, in the preoperative and immediate postoperative phase, to understand if the strength gains observed here can be replicated in people with hip osteoarthritis undergoing hip replacement surgery. In addition, future research is required to understand whether improvements to strength translate to an accelerated recovery from surgery, and greater participation in physical activity in the months and years following surgery. To produce reliable results, a blinded randomised controlled trial may be a suitable methodology to consider preventing researcher or participant level biases. The outcome measures used and described in Chapter 8 can be utilised in future research, and when combined with

measures of postoperative recovery, will help to understand how the use of NMES can influence factors such as the achievement of discharge criteria and length of stay. A longitudinal design is required, so that the effects of NMES can be maintained and translated into improvements to activity participation. Evaluations of cost effectiveness of NMES therapy compared to current practice may also be useful to inform implementation and adoption into healthcare settings. Finally, evaluations of adherence to NMES interventions need to be conducted longer-term and will be useful to inform the design of strategies to increase adherence to NMES interventions in the long-term.

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Appendices

Appendix 1. Experimental study 1 - Bournemouth University research ethics checklist

Bournemouth University

Research Ethics Checklist

About Your Checklist	
Ethics ID	27803
Date Created	03/08/2019 14:57:41
Status	Approved
Date Approved	05/09/2019 09:59:10
Date Submitted	04/09/2019 16:01:30
Risk	Low

Researcher Details	
Name	Louise Burgess
Faculty	Faculty of Health & Social Sciences
Status	Postgraduate Research (MRes, MPhil, PhD, DProf, EngD, EdD)
Course	Postgraduate Research - HSS
Have you received funding to support this research project?	No

Project Details	
Title	A lower limb comparison of older adults with osteoarthritis of the hip and healthy age-matched controls
Start Date of Project	01/09/2019
End Date of Project	01/12/2019
Proposed Start Date of Data Collection	01/10/2019
Original Supervisor	Ian Swain
Approver	Martin Hind

Summary - no more than 600 words (including detail on background methodology, sample, outcomes, etc.)

Total hip replacement, also termed total hip arthroplasty, is a surgical procedure that replaces the hip joint with an artificial prosthesis and has for some time been recognised as a clinically successful and cost-effective surgical procedure. Immediately following surgery, patients often exhibit a diminished ability to activate the lower limb muscles and may experience instability and strength deficits of both the operated and contralateral leg. As well as activation of muscles via the bodies' nervous system, muscles can also be contracted by the application of an external electrical stimulation. There is a traditional preference of voluntary, resisted exercise over electrical stimulation for strength improvement. However, as technology and research develops, electrical stimulation is becoming an increasingly attractive adjunct modality post-surgery.

The use of electrical muscle stimulation is still controversial in clinical practice due to the lack of guidelines on stimulation interventions and parameters, uncertainty regarding the efficacy of stimulation for strengthening muscles and concerns of pain in patients particularly sensitive to electrical stimulation. Whilst there is more research in this area in knee procedures, the mechanisms underlying weakness surrounding total hip replacement have not been examined to the same extent as in the knee replacement population. Further

investigation of electrical stimulation devices has been warranted, with particular focus to their use immediately post-surgery and in accelerating the recovery of muscle function during post-discharge rehabilitation. Therefore, this study aims to investigate the muscle weakness demonstrated in adults with hip osteoarthritis, and the potential role of electrical stimulation for improving recovery from surgery. The study with aim to recruit 12 healthy adults aged over 60 years old and 12 adults with end-stage osteoarthritis of the hip.

Hypotheses:

1) Participants presenting with hip osteoarthritis will have muscle weakness of the lower limbs when compared to healthy, age matched controls.

2) The lower limb muscles of participants with hip osteoarthritis will fatigue quicker when compared to healthy, age matched controls.

3) Participants presenting with hip osteoarthritis will have a reduction in muscle depth compared to healthy, age matched-controls.

4) Electrical muscle stimulation may play a role in strengthening weakened muscles.

This study will include the collection of biographical information, test results (lower limb strength, fatigue and function) and a short questionnaire. Participants will be invited to attend a testing session at the Orthopaedic Research Institute, Bournemouth University. Participant will perform a warm up, and then complete a series of lower limb strength tests using the PRIMUS RS multimodal dynamometer. Muscle fatigue of the quadriceps will be measured bilaterally through a fatigability test. The 30 second chair stand test, 40 metre fast paced walk test and the stair climb test will be completed. Lastly, this study will explore whether electrical muscle stimulation is acceptable and feasible for individuals with hip osteoarthritis by testing the device on the study participants, and asking for their feedback regarding discomfot.

Filter Question: Does your study involve Human Participants?

Participants

Describe the number of participants and specify any inclusion/exclusion criteria to be used	
12 healthy adults over 60 12 adults with a diagnosis of clinical hip osteoarthritis Exclusion Neurological disease affecting walking Rheumatoid arthritis Fitted with a pacemaker;Uncontrolled epilepsy; Loss of abductor musculature or poor skin coverage around the hip joint;Sepsis or osteomyelitis;Known metastatic tumour involving hip;Poor skin condition that prevents the use of electrodes;Not physically able to use testing equipment;Unable to provide informed consent.	
Do your participants include minors (under 16)?	
Are your participants considered adults who are competent to give consent but considered vulnerable?	No
Is a Disclosure and Barring Service (DBS) check required for the research activity?	No

Recruitment

Please provide details on intended recruitment methods, include copies of any advertisements.	
Potential participants will be randomly recruited using marketing tools such as posters, flyers and Twitter posts, shared on the University channels, and at local leisure centres. These channels will be accessed through connections at the Orthopaedic Research Institute, BU. Those interested in the study will be encouraged to contact the lead researcher for more information. Once an individual has expressed an interest, they will be sent a participant information sheet and consent form.	
Do you need a Gatekeeper to access your participants?	No

Data Collection Activity

Will the research involve questionnaire/online survey? If yes, don't forget to attach a copy of the questionnaire/survey or sample of questions.	Yes
How do you intend to distribute the questionnaire?	

other	
If Other, please provide details.	
This study will include the collection of biographical information, test results (lower limb strength, fatigue and function) and a short questionnaire	
Will the research involve interviews? If Yes, don't forget to attach a copy of the interview questions or sample of questions	
Will the research involve a focus group? If yes, don't forget to attach a copy of the focus group questions or sample of questions.	No
Will the research involve the collection of audio materials?	No
Will your research involve the collection of photographic materials?	No
Will your research involve the collection of video materials/film?	No
Will the study involve discussions of sensitive topics (e.g. sexual activity, drug use, criminal activity)?	No
Will any drugs, placebos or other substances (e.g. food substances, vitamins) be administered to the participants?	No
Will the study involve invasive, intrusive or potential harmful procedures of any kind?	No
Could your research induce psychological stress or anxiety, cause harm or have negative consequences for the participants or researchers (beyond the risks encountered in normal life)?	No
Will your research involve prolonged or repetitive testing?	No

Consent

Describe the process that you will be using to obtain valid consent for participation in the research activities. If consent is not to be obtained explain why.	
Once an individual has expressed an interest in taking part, they will be sent a participant information sheet and consent form before being asked to provide their fully informed consent to take part in the study. The contact details of the lead researcher will be on both of these forms, so that the individual can ask any questions before making a decision on participation.	
Do your participants include adults who lack/may lack capacity to give consent (at any point in the study)?	
Will it be necessary for participants to take part in your study without their knowledge and consent?	No

Participant Withdrawal

At what point and how will it be possible for participants to exercise their rights to withdraw from the study?
The participant will be told in the participant information sheet, and at the testing session, that they are free to withdraw at any time, without giving a reason.
If a participant withdraws from the study, what will be done with their data?
Information enabling direct/immediate identification (name, contact details, date of birth) will not be accessible to the research personnel for this study. No personal identifiable information will be recorded on any data collection documentation. All research data will be stored securely in adherence with the data protection legislation in force. If a participant withdraws, their anonymised data and research documentation will be deleted/shredded.

Participant Compensation

Will participants receive financial compensation (or course credits) for their participation?	Yes
Please provide details	
Participants will be offered a £10 Amazon voucher for taking part in the study.	
Will financial or other inducements (other than reasonable expenses) be offered to participants?	No
If participants choose to withdraw, how will you deal with compensation?	
Participants will receive their £10 Amazon voucher after attending the testing morning. If the participant decides they do not wish to be involved in the study after this point, their Amazon voucher will not be withdrawn.	

Research Data

Will identifiable personal information be collected, i.e. at an individualised level in a form that identifies or could enable identification of the participant?	No
Will research outputs include any identifiable personal information i.e. data at an individualised level in a form which identifies or could enable identification of the individual?	

Storage, Access and Disposal of Research Data

Where will your research data be stored and who will have access during and after the study has finished.	
Once your project completes, will any anonymised research data be stored on BU's Online Research Data Repository "BORDaR"?	No
Please explain why you do not intend to deposit your research data on BORDaR? E.g. do you intend to deposit your research data in another data repository (discipline or funder specific)? If so, please provide details.	

Dissemination Plans

Will you inform participants of the results?	

Final Review

Are there any other ethical considerations relating to your project which have not been covered above?	

Risk Assessment

Have you undertaken an appropriate Risk Assessment?	Yes

Attached documents

Participant Agreement Form.docx - attached on 04/09/2019 15:49:15
Participant Information Sheet .docx - attached on 04/09/2019 15:49:22
Research Participant Privacy Notice.pdf - attached on 04/09/2019 15:49:24
Oxford Hip Score.doc - attached on 16/09/2019 16:27:56
PASE_Questionnaire-2.pdf - attached on 16/09/2019 16:27:56

Approved Amendments	
Message	Good Afternoon, Please may I request an amendment to the approved ethics checklist? The amendment would involve adding two questionnaires to the data collection process. The first is the Physical Activity Scale for the Eldery (PASE), which assesses physical activity in older adults. It uses frequency, duration, and intensity level of activity over the previous week to assign a score, ranging from 0 to 793, with higher scores indicating greater physical activity. If accepted, this questionnaire will be used for both the osteoarthritis and healthy participants, so that we can compare activity levels between study groups.The second proposed questionnaire is the Oxford Hip Score, which is a short, 12-item patient reported outcome measure specifically designed and developed to assess function and pain in patients with hip osteoarthritis. It is an important addition to this research study so that we can quantify the severity of arthritis for the 12 participants in the hip osteoarthritis group. Licenses for both questionnaires have been requested.Thank you for considering the amendment. Best wishes,Louise
Date Submitted	16/09/2019 16:27
Comment	Thanks very much for this amendment request; Both questionnaires look fine and I am very happy to approve forthwith.NB. I note the Oxford HS example has Hospital Number and Name options on it, I assume that will be removed prior to use and replaced with your unique code?. Can you confirm that by email to mhind@bournemouth.ac.uk rather than you needing to repeat this BURE submission process.Many thanks Louise.Martin Hind FHSS Ethics Champion 16.9.19.
Date Approved	16/09/2019 20:22
Approved By	Martin Hind

Appendix 2. Experimental study 1 - Participant information sheet

Bournemouth University

Participant Information Sheet

The title of the research project

A lower limb comparison of older adults with osteoarthritis of the hip and healthy age-matched controls

Invitation to take part

We would like to invite you to take part in this research study which is being undertaken by Bournemouth University. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Who is organising the research?

The study is being organised by a PhD student at Bournemouth University.

What is the purpose of the project?

This study aims to investigate the muscle weakness demonstrated in adults with hip osteoarthritis, compared to healthy people the same age, and the potential role of electrical stimulation for helping to strengthen these muscles.

Why have I been chosen?

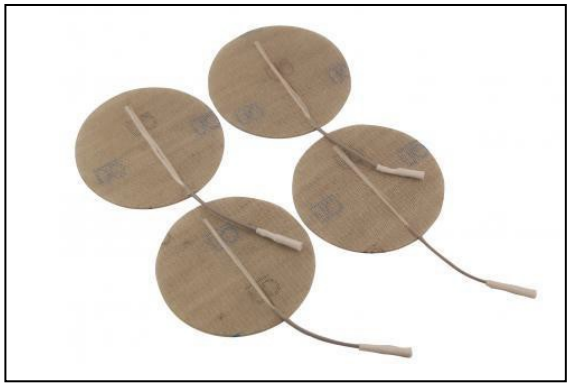
You are asked to take part in this study because you are aged over 60 years old and have either i) hip osteoarthritis or ii) with no musculoskeletal or neurological disorders. We are looking to include 12 participants in each group.

We won't be able to include you if you have any of the following relevant medical history:

A neurological disease affecting walking;
Rheumatoid arthritis;
Fitted with a pacemaker;
Uncontrolled epilepsy;
Sepsis or osteomyelitis;
Known metastatic tumour involving hip;
Poor skin condition that prevents the use of electrodes.

What is the electrical stimulation device?

The device is a Microstim neuromuscular stimulator, made by Odstock Medical Ltd. It is the size of a mobile phone and is connected to the muscles in your leg using two self-adhesive pads called electrodes.



When switched on, it produces electrical impulses which cause a comfortable, involuntary contraction of the quadriceps muscles. There is lots of research in this area for knee replacement patients, but less for those undergoing hip replacement. Therefore we are testing the feasibility of using it in a population of patients with hip osteoarthritis.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a participant agreement form. You can withdraw from participation during the study at any time and without giving a reason. If you decide to withdraw we will usually remove any data collected about you from the study. Once the data collection has finished you may still be able to withdraw your data up to the point where the data is analysed and incorporated into the research findings or outputs. At this point your data will usually become anonymous, so your identity cannot be determined, and it may not be possible to identify your data within the anonymous dataset. Withdrawing your data at this point may also adversely affect the validity and integrity of the research. Deciding to take part or not will not adversely impact your future treatment.

What would taking part involve?

You will be invited to attend a testing session at the Orthopaedic Research Institute, Bournemouth University, where we will collect some data on your leg strength and functional ability (stair climbing, walking speed, getting up and down from a chair). We will also ask you to have a go at using our electrical muscle stimulation device on your quadriceps and gluteal muscles, to see if you find it comfortable or not. The testing session would take around one hour of your time.

What are the advantages and possible disadvantages or risks of taking part?

Whilst there are no immediate benefits for those people participating in the project, it is hoped that this work will help to inform future treatment decisions for people with osteoarthritis. You will not be paid for your participation in this study. However, reimbursement of reasonable travel expenses can be arranged, or we can send you a £20 gift card to say thank you.

There may be some discomfort from the stimulation and there is a small risk of skin irritation.

What type of information will be sought from me and why is the collection of this information relevant for achieving the research project's objectives?

We will ask you to complete a series of lower limb strength tests using a manual muscle tester. We will measure how quickly it takes your quadriceps muscles to tire. We will also test your functional ability, which will include getting up and down from a chair, walking and climbing stairs. Lastly, we will ask you to have a go at using our electrical muscle stimulation device on your quadriceps and gluteal muscles, to see if you find it comfortable or not. The results from the osteoarthritis group will be compared to the results from the group of adults without osteoarthritis, in order to inform future research in this area.

How will my information be kept?

All the information we collect about you during the course of the research will be kept strictly in accordance with current data protection legislation. Research is a task that we perform in the public interest, as part of our core function as a university. Bournemouth University (BU) is a Data Controller of your information which means that we are responsible for looking after your information and using it appropriately. BU's Research Participant Privacy Notice sets out more information about how we fulfil our responsibilities as a data controller and about your rights as an individual under the data protection legislation. We ask you to read this Notice so that you can fully understand the basis on which we will process your information.

Publication

You will not be able to be identified in any external reports or publications about the research without your specific consent. Otherwise your information will only be included in these materials in an anonymous form, i.e. you will not be identifiable.

Research results will be published in an academic journal, and in the PhD thesis in which the study is a part of.

Security and access controls

BU will hold the information we collect about you in hard copy in a secure location and on a BU password protected secure network where held electronically.

Except where it has been anonymised your personal information will be accessed and used only by appropriate, authorised individuals and when this is necessary for the purposes of the research or another purpose identified in the Privacy Notice. This may include giving access to BU staff or others responsible for monitoring and/or audit of the study, who need to ensure that the research is complying with applicable regulations.

Retention of your data

All personal data collected for the purposes of this study will be held for 5 years from the date of publication of the research or presentation of the results to the sponsor, whichever is later/ 5 year after the award of the degree. Although published research outputs are anonymised, we need to retain underlying data collected for the study in a non-anonymised form for a certain period to enable the research to be audited and/or to enable the research findings to be verified.

Contact for further information

If you have any questions or would like further information, please contact Louise Burgess (PhD student) on 01202 961651 or lburgess@bournemouth.ac.uk or Ian Swain (supervisor) on 01202 964010 or iswain@bournemouth.ac.uk.

In case of complaints

Any concerns about the study should be directed to Vanora Hundley, Faculty of Health and Social Sciences, Bournemouth University by email to researchgovernance@bournemouth.ac.uk.

Finally

If you decide to take part, you will be given a copy of the information sheet and a signed participant agreement form to keep.

Thank you for considering taking part in this research project.

Appendix 3. Experimental study 1 - Consent form

Lower Limb Comparison Participant Agreement Form v2
Ethics ID: 27803
Date: 04/09/2019

Bournemouth University

Participant Agreement Form

Full title of project: A lower limb comparison of older adults with osteoarthritis of the hip and healthy age-matched controls

Name, position and contact details of researcher: Louise Burgess, PhD Student (01202 961651, lburgess@bournemouth.ac.uk)

Name, position and contact details of supervisor: Ian Swain, Professor in Clinical Engineering (01202 964010, iswain@bournemouth.ac.uk)

To be completed prior to data collection activity

Agreement to participate in the study

You should only agree to participate in the study if you agree with all of the statements in this table and accept that participating will involve the listed activities.

I have read and understood the Participant Information Sheet (Lower Limb Comparison v2, dated 4th September 2019) and have been given access to the BU Research Participant Privacy Notice which sets out how we collect and use personal information (https://www1.bournemouth.ac.uk/about/governance/access-information/data-protection-privacy).	
I have had an opportunity to ask questions.	
I understand that my participation is voluntary. I can stop participating in research activities at any time without giving a reason and I am free to decline to answer any particular question(s).	
I understand that taking part in the research will include the following activity/activities as part of the research:	
Collection of data on my height, weight, age and past medical history	
Collection of data on my leg strength	
Collection of data on my walking speed, ability to get up and down from a chair, and climb stairs.	
Use of an electrical stimulation device on my legs	
Feedback on the use of an electrical stimulation device.	
I understand that, if I withdraw from the study, I will also be able to withdraw my data from further use in the study **except** where my data has been anonymised (as I cannot be identified) or it will be harmful to the project to have my data removed.	
I understand that my data may be used in an anonymised form by the research team to support other research projects in the future, including future publications, reports or presentations.	
	Initial box to agree
I consent to take part in the project on the basis set out above	

I confirm my agreement to take part in the project on the basis set out above.

Name of participant (BLOCK CAPITALS)	Date (dd/mm/yyyy)	Signature

Name of researcher (BLOCK CAPITALS)	Date (dd/mm/yyyy)	Signature

Appendix 4. Oxford Hip Score

Problems with your hip

During the past 4 weeks..

✓tick one box for every question.

1. ***During the past 4 weeks***.....

How would you describe the pain you usually had from your hip?

None	Very mild	Mild	Moderate	Severe
❑	❑	❑	❑	❑

2. ***During the past 4 weeks***.....

Have you had any trouble with washing and drying yourself (all over) because of your hip?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❑	❑	❑	❑	❑

3. ***During the past 4 weeks***.....

Have you had any trouble getting in and out of a car or using public transport because of your hip? *(whichever you tend to use)*

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❑	❑	❑	❑	❑

4. ***During the past 4 weeks***.....

Have you been able to put on a pair of socks, stockings or tights?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

5. ***During the past 4 weeks***.....

Could you do the household shopping on your own?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

6. ***During the past 4 weeks***.....

For how long have you been able to walk before pain from your hip becomes severe? (*with or without a stick)*

No pain/ More than 30 minutes	16 to 30 minutes	5 to 15 minutes	Around the house only	Not at all -pain severe on walking
❑	❑	❑	❑	❑

P.T.O./

During the past 4 weeks...

✓tick one box for every question

7 ***During the past 4 weeks*****.....**

Have you been able to climb a flight of stairs?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

8 ***During the past 4 weeks*****.....**

After a meal (sat at a table), how painful has it been for you to stand up from a chair because of your hip?

Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
❑	❑	❑	❑	❑

9 ***During the past 4 weeks*****.....**

Have you been limping when walking, because of your hip?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
❑	❑	❑	❑	❑

10 ***During the past 4 weeks*****.....**

Have you had any sudden, severe pain - 'shooting', 'stabbing' or 'spasms' - from the affected hip?

No days	Only 1 or 2 days	Some days	Most days	Every day
❑	❑	❑	❑	❑

11 ***During the past 4 weeks*****.....**

How much has pain from your hip interfered with your usual work *(including housework)*?

Not at all	A little bit	Moderately	Greatly	Totally
❑	❑	❑	❑	❑

12 ***During the past 4 weeks*****.....**

Have you been troubled by pain from your hip in bed at night?

No nights	Only 1 or 2 nights	Some nights	Most nights	Every night
❑	❑	❑	❑	❑

Appendix 5. Physical activity scale for the elderly (PASE)

LEISURE TIME ACTIVITY

1. Over the past 7 days, how often did you participate in sitting activities such as reading, watching TV or doing handcrafts?

[0.] NEVER	[1.] SELDOM (1-2 DAYS)	[2.] SOMETIMES (3-4 DAYS)	[3.] OFTEN (5-7 DAYS)
↓	↓	↓	↓
GO TO Q.#2			

1a. What were these activities?

_____

1b. On average, how many hours per day did you engage in these sitting activities?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

2. Over the past 7 days, how often did you take a walk outside your home or yard for any reason? For example, for fun or exercise, walking to work, walking the dog, etc.?

[0.] NEVER	[1.] SELDOM (1-2 DAYS)	[2.] SOMETIMES (3-4 DAYS)	[3.] OFTEN (5-7 DAYS)
↓	↓	↓	↓
GO TO Q.#3			

2a. On average, how many hours per day did you spend walking?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

3. Over the past 7 days, how often did you engage in light sport or recreational activities such as bowling, golf with a cart, shuffleboard, fishing from a boat or pier or other similar activities?

[0.] NEVER	[1.] SELDOM (1-2 DAYS)	[2.] SOMETIMES (3-4 DAYS)	[3.] OFTEN (5-7 DAYS)
↓	↓	↓	↓
GO TO Q.#4			

3a. What were these activities?

_____

3b. On average, how many hours per day did you engage in these light sport or recreational activities?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

4. Over the past 7 days, how often did you engage in moderate sport and recreational activities such as doubles tennis, ballroom dancing, hunting, ice skating, golf without a cart, softball or other similar activities?

[0.] NEVER	[1.] SELDOM (1-2 DAYS)	[2.] SOMETIMES (3-4 DAYS)	[3.] OFTEN (5-7 DAYS)
↓	↓	↓	↓
GO TO Q.#5			

4a. What were these activities?

_____

4b. On average, how many hours per day did you engage in these moderate sport and recreational activities?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

5. Over the past 7 days, how often did you engage in strenuous sport and recreational activities such as jogging, swimming, cycling, singles tennis, aerobic dance, skiing (downhill or cross-country) or other similar activities?

[0.] NEVER	[1.] SELDOM	[2.] SOMETIMES	[3.] OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q.#6	↓	↓	↓

5a. What were these activities?

_____

5b. On average, how many hours per day did you engage in these strenuous sport and recreational activities?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

6. Over the past 7 days, how often did you do any exercises specifically to increase muscle strength and endurance, such as lifting weights or pushups, etc.?

[0.] NEVER	[1.] SELDOM	[2.] SOMETIMES	[3.] OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q.#7	↓	↓	↓

6a. What were these activities?

_____

6b. On average, how many hours per day did you engage in exercises to increase muscle strength and endurance?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

HOUSEHOLD ACTIVITY

7. During the past 7 days, have you done any light housework, such as dusting or washing dishes?

[1.] NO [2.] YES

8. During the past 7 days, have you done any heavy housework or chores, such as vacuuming, scrubbing floors, washing windows, or carrying wood?

[1.] NO [2.] YES

9. During the past 7 days, did you engage in any of the following activities?

Please answer YES or NO for each item.

		NO	YES
a.	Home repairs like painting, wallpapering, electrical work, etc.	1	2
b.	Lawn work or yard care, including snow or leaf removal, wood chopping, etc.	1	2
c.	Outdoor gardening	1	2
d.	Caring for an other person, such as children, dependent spouse, or an other adult	1	2

WORK-RELATED ACTIVITY

10. During the past 7 days, did you work for pay or as a volunteer?

[1.] NO [2.] YES

10a. How many hours per week did you work for pay and/or as a volunteer?

_____ HOURS

10b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work?

[1] Mainly sitting with slight arm movements. [**Examples:** office worker, watchmaker, seated assembly line worker, bus driver, etc.]

[2] Sitting or standing with some walking. [**Examples:** cashier, general office worker, light tool and machinery worker.]

[3] Walking, with some handling of materials generally weighing less than 50 pounds. [**Examples:** mailman, waiter/waitress, construction worker, heavy tool and machinery worker.]

[4] Walking and heavy manual work often requiring handling of materials weighing over 50 pounds. [**Examples:** lumberjack, stone mason, farm or general laborer.]

Appendix 6. Adherence review PROSPERO registration

PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

A list of fields that can be edited in an update can be found here

1. * Review title.

Give the title of the review in English

Strategies to increase adherence in electrical stimulation interventions for muscle weakness in osteoarthritis: a systematic review

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

01/12/2020

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

01/02/2021

5.1 * Stage of review at time of this submission.

This field uses answers to initial screening questions. It cannot be edited until after registration.

Tick the boxes to show which review tasks have been started and which have been completed.

Update this field each time any amendments are made to a published record.

The review has not yet started: No

Review stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Louise Burgess

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Miss Burgess

7. * Named contact email.

Give the electronic email address of the named contact.

lburgess@bournemouth.ac.uk

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

The Orthopaedic Research Institute, Executive Business Centre, Bournemouth University, 89 Holdenhurst Road, Bournemouth BH8 8EB

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

+44 (0)1202 961651

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Bournemouth University

Organisation web address:

[11.change] Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record.**

Miss Louise Burgess. Bournemouth University
Professor Ian Swain. Bournemouth University
Professor Paul Taylor. Bournemouth University
Mr Shayan Bahadori. Bournemouth University
Professor Tom Wainwright. Bournemouth University

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

No study-specific funding has been received for this review

Grant number(s)

State the funder, grant or award number and the date of award

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

i) To quantify the levels of adherence in NMES (neuromuscular electrical stimulation) interventions for muscle weakness in hip and knee osteoarthritis;

ii) To identify reasons for adherence and non-adherence; and

iii) To identify strategies to increase adherence.

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

A web-based literature search was completed in December 2020 and the databases sourced included the Cochrane Library, CINAHL Complete, MEDLINE Complete and PubMed, accessed through Bournemouth University's online library.

Randomised and non-randomised clinical trials, pilot studies, retrospective analyses and case-reports were

included, given the paucity of evidence in the area of NMES and osteoarthritis.

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Hip and knee osteoarthritis.

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Cohorts of adults with hip or knee osteoarthritis (both the non-surgical and surgical population).

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

A protocol of electrical muscle stimulation prescribed to increase muscle strength.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Not applicable.

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Randomised and non-randomised clinical trials, pilot studies, retrospective analyses and case-reports will be included, given the paucity of evidence in the area of NMES and osteoarthritis.

Studies will include adults with hip or knee osteoarthritis (both the non-surgical and surgical population).

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Adherence to study intervention.

Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Percentage of adherence to study intervention.

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

Strategies to monitor adherence; reasons for adherence and non-adherence and outcomes from the study.

Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Not applicable.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Selected studies will be screened based on their title and abstract. Full-text screening will be conducted by two members of the research team.

Data will then be extracted from the included manuscripts onto extraction sheets developed in Microsoft Excel.

The following data will be extracted: i) study design; ii) study population (sample size, type of osteoarthritis, and whether they were surgical or non-surgical patients; iii) NMES dose; iv) adherence; v) strategies to monitor adherence; vi) reasons for adherence and non-adherence and vii) outcomes from the study.

In addition, adverse events or dropouts from the trial that are clearly related to the NMES intervention will be recorded.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

The Downs and Black checklist will be used to assess the risk of bias within the studies yielded in this review. The 27-item checklist was chosen as it is suitable for the appraisal of both randomised and non-randomised clinical trials, and has been shown to have good intra-rater and inter-rater reliability.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be

specific to your review and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

The heterogenous nature of the included studies, and the different methods used for measuring adherence will prevent the use of meta-analysis. Descriptive statistics will be used to summarise the characteristics of the studies and adherence rates.

Data on strategies to monitor adherence; reasons for adherence and non-adherence will be thematically analysed using an inductive approach to identify key themes.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

None planned.

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness
No

Diagnostic
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
No

Intervention
Yes

Living systematic review
No

Meta-analysis
No

Methodology
No

Narrative synthesis
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
No

Prospective meta-analysis (PMA)
No

Review of reviews
No

Service delivery
No

Synthesis of qualitative studies
No

Systematic review
Yes

Other
No

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

COVID-19
No

Crime and justice
No

Dental
No

Digestive system
No

Ear, nose and throat
No

Education
No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions
No

Musculoskeletal
Yes

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
Yes

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
Yes

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
No

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

England

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

We plan to publish the findings of this review in a suitable, peer-reviewed medical journal.

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

Electrical muscle stimulation; Knee osteoarthritis; Hip osteoarthritis; Joint replacement surgery; Adherence

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.
Please provide anticipated publication date

Review_Completed_published

39. Any additional information.

Provide any other information relevant to the registration of this review.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission). List authors, title and journal details preferably in Vancouver format.

https://PubMed.ncbi.nlm.nih.gov/34262384/

Give the link to the published review or preprint.

Appendix 7. NMES instructions

1. Introduction

You are enrolled onto a study to evaluate the effects of Neuromuscular Electrical Stimulation (NMES) on your quadriceps strength. Thank you for taking part in this study.

This document includes all the information you need to be able to apply the NMES device on yourself at home. You will be shown how to do this during your baseline assessment at the Orthopaedic Research Institute, Bournemouth University.

You will be contacted by phone every two weeks to have the intervention reviewed. If at any time you have any questions about the study or NMES device or need to report any adverse events, please contact the lead researcher using the contact details below. Please remember to complete your NMES diary after every session.

Louise Burgess
01202 961651 (Monday-Friday 8am-4pm)
Outside of these hours: 07496 655610
Email: lburgess@bournemouth.ac.uk

2. Frequently Asked Questions

2.1 What is neuromuscular electrical stimulation?

Neuromuscular electrical stimulation sends electrical impulses to nerves. This causes muscles to contract. Doing so can increase muscle strength and offset the effects of muscle disuse. It is often use to re-train or re-educate a muscle to function and to build strength before or after surgery or following a period of disuse.

2.2 What device will be used in this study?

The device used in this study is a Microstim neuromuscular stimulator, made by Odstock Medical Ltd. It is the size of a mobile phone and is connected to the muscles in your leg using two self-adhesive pads called electrodes.

Odstock Medical Orthopaedic Stimulator

This stimulator includes programmes to improve venous return to reduce swelling and prevent thrombosis, pain relief modes similar to a TENS machine, as well as specific programmes to improve either muscle power or fatigue resistance.

2.3 Is the device safe?

The NMES device itself is not under investigation as it has already passed external safety testing. Therefore, no adverse device effects are anticipated.

2.4 What will the device do?

Research evidence conducted with a variety of patient groups and athletes has found that NMES can improve muscle size and strength. However, very little work has been done in this area and muscle endurance with older adults and therefore we are testing whether using endurance settings on the device will improve muscle endurance.

2.5 How often do I use the device?

Please try to follow the NMES training schedule we have given you. This starts with 2 x 15 minutes sessions a day, 5 times per week. The length of these sessions increases to 30 minutes by the last week.

2.6 What happens if I miss an NMES session?

If you have a busy week, and are unable to complete every session, please do not worry. Please just make a note in your NMES diary when you were unable to complete the session.

2.7 Will the electrodes irritate my skin?

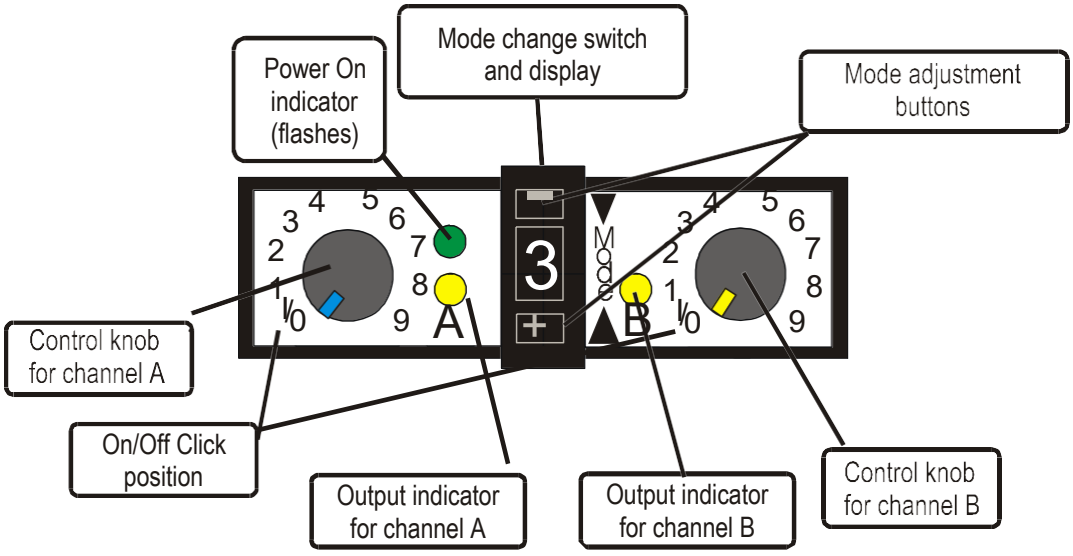
It is common for the skin to go a little red after electrode use. This redness is nothing to worry about and should disappear by itself after 30 minutes. If experienced any skin irritation other than redness, please let the lead researcher know.

2.8 What are rest days?

Rest days are rest from using the NMES device. These are important so that your muscles have chance to recover. Please continue with any other activities as you usually would.

3. Operating the device

The device has been pre-programmed with 9 modes that are personalised to have various therapeutic effects. In this study, we aim to improve muscle endurance, so will ask you to use mode 7 at all times. The mode can be set using the + and – buttons at the bottom of the stimulator, as shown in the image below.



Orthopaedic Stimulator switches

The stimulator has two different channels, which means we can apply NMES to your left and right leg at the same time. As you will see in the picture above, the dial on the left controls the stimulation intensity of channel A, and the dial on the right controls the stimulation intensity of channel B. Each number on the dial corresponds to approximately 10 milliamp (mA) of electrical current. It Is important that these dials are turned up slowly, so that you can adjust the stimulation intensity to suit your pain threshold. The intensity needs to be sufficient to produce an involuntary muscle contraction, however, should not be painful. You should try to apply the same intensity of stimulation to both legs.

Please do not move the electrodes while the device is switched on.

4. Applying the device to your quadriceps

The device activates your muscles through electrodes placed over the muscle belly. These electrodes can be reused until they lose their stickiness, and we will give you some replacements for when this happens.

To help maintain the stickiness of the electrodes, please dampen them regularly (when not attached to the NMES device) by running water over the surface of the sticky side.

Prior to applying the electrodes to your skin, make sure your skin is clean and free of any moisturiser or cream.

Connect the electrodes to the leads of the stimulation by inserting the pin into the connector of the flying leads of the electrodes.

Peel the electrode away from the plastic sheet by lifting at the electrode edge. Do not pull the flying lead.

Place the electrodes on the skin in the positions shown in the diagram below. These points will be marked on your skin during your baseline assessment to help with accuracy.

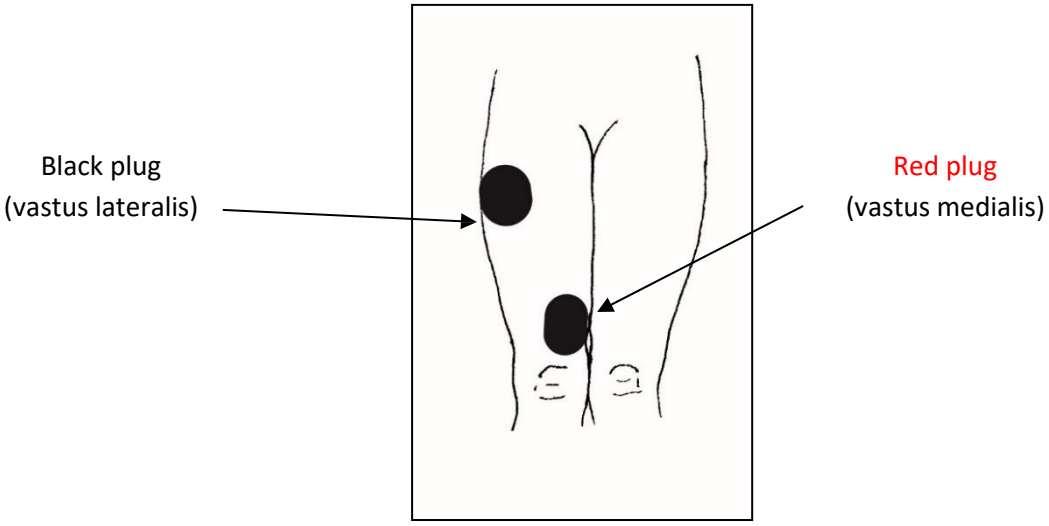
The electrode with the black plug is the active electrode. This must be placed on the higher point of your quadriceps (origin of the vastus lateralis).

The electrode with the red plug is the indifferent electrode. This should be placed over the vastus medialis as shown in the diagram below.

After use, peel the electrode away from the skin by lifting the edge. Do not pull the lead.

Replace the electrodes on their plastic sleeve by running a wetted finger over the sticky side of the electrode. Then place the electrode back on the plastic sleeve on the side that reads ON. It will read NO if it is the wrong side.

Please remember to turn the stimulation off before handling the electrodes.



Electrode placement on the quadriceps.

5. Battery

A 9V PP3 alkaline non-rechargeable or equivalent rechargeable battery should be used in the device. The device will have a new battery in it when it is given for you, which should last between 6-12 weeks. When the battery nears exhaustion a low battery warning will occur. During an exercise period the stimulator will automatically reduce the stimulus output to zero and then bleep and flash the power indicator for approximately thirty seconds. After this time the stimulator will enter 'sleep' mode and should be switched OFF before replacing the battery.

Appendix 8. NMES diary extract

Week 2

Day *Insert date*	**Prescribed NMES dose**	**Actual dose**	**Current intensity** *Dial number*	**Muscle contraction achieved?** *Yes or No*	**Discomfort level (0-10)** *0=no discomfort 10=unbearable*
Day 1	**2 x 20-minute sessions** **Device setting:** 7 **Intensity:** Sufficient to induce visible quadriceps contraction.		Channel A: Channel B:		
Day 2	**2 x 20-minute sessions** **Device setting:** 7 **Intensity:** Sufficient to induce visible quadriceps contraction.		Channel A: Channel B:		
Day 3	**Rest**				
Day 4	**2 x 20-minute sessions** **Device setting:** 7 **Intensity:** Sufficient to induce visible quadriceps contraction.		Channel A: Channel B:		
Day 5	**2 x 20-minute sessions** **Device setting:** 7 **Intensity:** Sufficient to induce visible quadriceps contraction.		Channel A: Channel B:		
Day 6	**Rest**				
Day 7	**2 x 20-minute sessions** **Device setting:** 7 **Intensity:** Sufficient to induce visible quadriceps contraction.		Channel A: Channel B:		

Week 2 RPE:

Week 2 notes:

Appendix 9. Experimental study 2 – Bournemouth University ethics

Bournemouth University

Research Ethics Checklist

About Your Checklist	
Ethics ID	38615
Date Created	21/05/2021 14:21:54
Status	Approved
Date Approved	25/08/2021 11:29:19
Date Submitted	16/07/2021 14:41:08
Risk	Low

Researcher Details	
Name	Louise Burgess
Faculty	Faculty of Health & Social Sciences
Status	Postgraduate Research (MRes, MPhil, PhD, DProf, EngD, EdD)
Course	Postgraduate Research - HSS
Have you received funding to support this research project?	No
Please list any persons or institutions that you will be conducting joint research with, both internal to BU as well as external collaborators.	Associate Professor Thomas Wainwright, Professor Ian Swain, Professor Paul Taylor

Project Details	
Title	Does neuromuscular electrical stimulation improve knee extensor muscle endurance in adults with hip osteoarthritis? A feasibility study.
Start Date of Project	01/09/2021
End Date of Project	01/01/2022
Proposed Start Date of Data Collection	01/09/2021
Original Supervisor	Ian Swain
Approver	Susan Dewhurst
Summary - no more than 600 words (including detail on background methodology, sample, outcomes, etc.)	
This study aims to determine whether neuromuscular electrical stimulation (NMES) can strengthen the quadriceps muscles of adults with hip osteoarthritis. This study is part of a wider project, which aims to investigate whether NMES can improve recovery from hip replacement surgery. NMES sends electrical impulses to nerves. This causes muscles to contract. Doing so can increase muscle strength and offset the effects of muscle disuse. NMES is often use to re-train or re-educate a muscle to function and to build strength before or after surgery or following a period of disuse. However, very little work has been done in this area and hip osteoarthritis patients. In the proposed study, adults with hip osteoarthritis will complete a 6-week intervention of home-based NMES, applied bilaterally to the	

quadriceps.

Participants diagnosed with hip osteoarthritis will be recruited from the local community. Those eligible to take part in the study will be invited to attend a baseline assessment at the Orthopaedic Research Institute, Bournemouth University. Data will be collected on osteoarthritis symptoms, knee extensor strength and endurance, functional performance, activities of daily living and quadriceps cross-sectional area. Participants will complete six weeks of NMES training at home. Participants will be contacted by telephone throughout the study, so they are able to report any adverse events or device deficiencies, and have their treatment reviewed. A diary and built-in tracker will be used to report device usage and adherence to the study protocol. Participants will be invited to attend a final assessment at seven weeks from their baseline appointment where their baseline measures will be repeated. In addition, participants will be asked to provide feedback on the acceptability and practicality of using the device, to assess the feasibility of the intervention. A pre-post analysis will be used to evaluate the effectiveness of NMES for improving knee extensor endurance, and subsequent functional performance, in adults with hip osteoarthritis. Six weeks after the intervention is complete, participants will be asked to complete two questionnaires on their levels of physical activity, and their hip symptoms, so we can evaluate the effects of NMES once the intervention is complete.

Filter Question: Does your study involve Human Participants?

Participants

Describe the number of participants and specify any inclusion/exclusion criteria to be used

Participants meeting all the following inclusion criteria will be considered for participation within the study:

- Male or female, aged 45 years or over, with a clinical diagnosis of unilateral or bilateral hip osteoarthritis (assessment from a physiotherapist or doctor, no radiological assessment required);
- Chronic joint pain for at least three months;
- Oxford Hip Score <40
- Independently mobile and able to carry out study protocol.

Participants will be excluded if they meet any of the following criteria:

- Neurological disease affecting walking ability (Parkinson's, cerebral palsy, multiple sclerosis, other spasticity);
- Rheumatoid arthritis;
- Fitted with a pacemaker or other active medical implant;
- Suffer from uncontrolled epilepsy;
- Sepsis or osteomyelitis;
- Known metastatic tumour involving the hip;
- Poor skin condition that prevents the use of self-adhesive electrodes;
- Not able to produce an involuntary muscle contraction of the quadricep muscles using NMES;
- Not physically able to use Primus muscle testing equipment, climb stairs or walk 40m;
- Are participating in any form of voluntary exercise to increase muscle strength;
- Unable to provide informed consent (insufficient English, cognitive disorder such as dementia, psychiatric illness);
- Unable to complete study follow up.

The study will aim to recruit 12 participants.

Do your participants include minors (under 16)?	No
Are your participants considered adults who are competent to give consent but considered vulnerable?	No
Is a Disclosure and Barring Service (DBS) check required for the research activity?	No

Recruitment

Please provide details on intended recruitment methods, include copies of any advertisements.

Twelve adults with a diagnosis of clinical hip osteoarthritis will be randomly recruited using marketing tools such as posters and Twitter

posts, shared on the University channels, at local leisure centres and physiotherapy centres. Those interested in the study will be asked to contact the lead researcher (LB) for more information. Once an individual has expressed an interest in taking part, they will be screened via a telephone call to ensure they meet the pre-determined eligibility criteria. Each participant will be advised that they are under no obligation to take part and can withdraw at any time without providing a reason. If the participant decides to proceed with the study, they will be asked to complete an informed consent form at their baseline assessment. Recruitment will continue until twelve participants have completed the study.

Do you need a Gatekeeper to access your participants?	No

Data Collection Activity	
Will the research involve questionnaire/online survey? If yes, don't forget to attach a copy of the questionnaire/survey or sample of questions.	Yes
How do you intend to distribute the questionnaire?	
face to face	
Will the research involve interviews? If Yes, don't forget to attach a copy of the interview questions or sample of questions	No
Will the research involve a focus group? If yes, don't forget to attach a copy of the focus group questions or sample of questions.	No
Will the research involve the collection of audio materials?	No
Will your research involve the collection of photographic materials?	No
Will your research involve the collection of video materials/film?	No
Will the study involve discussions of sensitive topics (e.g. sexual activity, drug use, criminal activity)?	No
Will any drugs, placebos or other substances (e.g. food substances, vitamins) be administered to the participants?	No
Will the study involve invasive, intrusive or potential harmful procedures of any kind?	No
Could your research induce psychological stress or anxiety, cause harm or have negative consequences for the participants or researchers (beyond the risks encountered in normal life)?	No
Will your research involve prolonged or repetitive testing?	No

Consent
Describe the process that you will be using to obtain valid consent for participation in the research activities. If consent is not to be obtained explain why.
Once an individual has expressed an interest in taking part, they will be sent a participant information sheet and consent form to read. The contact details of the lead researcher will be on both of these forms, so that the individual can ask any questions before making a decision on participation. Each participant will be advised that they are under no obligation to take part and can withdraw at any time without providing a reason. If the participant decides to proceed with the study, they will be asked to complete an informed consent form at their baseline assessment. To comply with Good Clinical Practice (GCP) guidelines, the research team member will ensure that the participant has time to consider their participation within the study, including time to ask questions, before written informed consent is collected. The research team member will review the participant's medical history to ensure there is no relevant medical history that needs to be considered, and complete study specific screening to ensure eligibility. The original signed consent form will be kept in the Investigator's Site File and participants will be provided with a copy.

Do your participants include adults who lack/may lack capacity to give consent (at any point in the study)?	No
Will it be necessary for participants to take part in your study without their knowledge and consent?	No

Participant Withdrawal

At what point and how will it be possible for participants to exercise their rights to withdraw from the study?

Participants will be withdrawn from the study if they lose capacity to comply with protocol requirements during the study or choose to withdraw. Discussion of the requirement to withdraw a participant will be performed by a member of the research team who will explain to each participant the reason they are being withdrawn. Participants who wish to stop the intervention early, but are willing to attend their follow-up assessment, will be invited to attend their second assessment early.

Every attempt will be made to ensure that all the research participants return for the follow up assessment. However, participants are free to withdraw from the study at any time and are under no obligation to provide a reason for doing so. Participants who withdraw from the study should have the reason for their withdrawal recorded on their Case Report Form (CRF).

If a participant withdraws from the study, what will be done with their data?

Information enabling direct/immediate identification (name, contact details, date of birth) will not be accessible to the research personnel for this study. No personal identifiable information will be recorded on any data collection documentation. All research data will be stored securely in adherence with the data protection legislation in force. If a participant withdraws and does not agree to attend their follow up appointment early, their anonymised data and research documentation will be deleted/shredded.

Participant Compensation

Will participants receive financial compensation (or course credits) for their participation?	Yes

Please provide details

Participants will receive a £20 John Lewis voucher for taking part in the study.

Will financial or other inducements (other than reasonable expenses) be offered to participants?	No

If participants choose to withdraw, how will you deal with compensation?

The £20 voucher will be given to the participant when they return to the Orthopaedic Research Institute for their follow up assessment. If they choose to withdraw before this, they will not receive the voucher.

Research Data

Will identifiable personal information be collected, i.e. at an individualised level in a form that identifies or could enable identification of the participant?	No
Will research outputs include any identifiable personal information i.e. data at an individualised level in a form which identifies or could enable identification of the individual?	No

Storage, Access and Disposal of Research Data

Where will your research data be stored and who will have access during and after the study has finished.

Data will be collected on an electronic case report form (eCRF), using a secure, web-based portal (Actipath). Data will be stored this database. All participants entered onto the database will be assigned a participant ID number, allowing for protection of the participant's identity. The database is restricted, user authentication is required to input or view research data and the amount of data that can be viewed by a user will be determined by their role, as defined in the data management plan and the delegation log. Any data entered to the database is managed with an audit trail that will record the username of all those entering and /or changing data in this study.

Information with regards to study participants will be kept confidential and managed in accordance with data protection legislation, the UK Policy Framework for Health and Social Care Research (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/) and Research Ethics Committee.

Once your project completes, will any anonymised research data be stored on BU's Online Research Data Repository "BORDaR"?	Yes

Dissemination Plans

How do you intend to report and disseminate the results of the study?	
Peer reviewed journals,Internal Report,Conference presentation,Publication on website,Public Engagement Activities	
Will you inform participants of the results?	Yes
If Yes or No, please give details of how you will inform participants or justify if not doing so	
Participants will be informed with the results of the study through a study report, completed once data analysis has occurred.	

Final Review

Are there any other ethical considerations relating to your project which have not been covered above?	No

Risk Assessment

Have you undertaken an appropriate Risk Assessment?	Yes

Attached documents

PROTOCOL Does neuromuscular electrical stimulation improve knee extensor muscle endurance in adults with hip osteoarthritis 14.07.21.docx - attached on 16/07/2021 14:37:24
Participant Agreement Form.docx - attached on 16/07/2021 14:37:29
Participant Information Sheet.docx - attached on 16/07/2021 14:37:32
Research Participant Privacy Notice.pdf - attached on 16/07/2021 14:37:36
HOOS.pdf - attached on 16/07/2021 14:37:46
NMES feedback questionnaire.docx - attached on 16/07/2021 14:37:48
System Usability Scale v1.docx - attached on 16/07/2021 14:37:51
Oxford Hip Score.pdf - attached on 16/07/2021 14:40:13
PASE_Questionnaire-2.pdf - attached on 16/07/2021 14:40:17
PROTOCOL Does neuromuscular electrical stimulation improve knee extensor muscle endurance in healthy older adults V1 30.03.22.03.22.docx - attached on 30/03/2022 11:27:31
Participant Information Sheet.docx - attached on 30/03/2022 11:27:31
Participant Agreement Form.docx - attached on 30/03/2022 11:27:31

Approved Amendments

Message	Dear Sir/Madam,We would like to request an amendment to the approved study "Does neuromuscular electrical stimulation (NMES) improve knee extensor muscle endurance in adults with hip osteoarthritis? A feasibility study". The requested changes are summarised below:-Recruitment of a healthy older adult population rather than a

	patient population.-Removal of hip arthritis specific outcome measures (pain, Oxford Hip Score, the Hip Disability and Osteoarthritis Outcome Score (HOOS)).-Change the NMES protocol from alternative contractions (one leg at a time) to simultaneous.-Change the study title to: “Does neuromuscular electrical stimulation improve knee extensor muscle endurance in healthy older adults? A feasibility study.”We have attached the updated study protocol and documents (participant information sheet and consent form). Please could you review this amendment and let us know if you’re happy for the study to resume?Thank you very much for your help.Best wishes,Louise Burgess
Date Submitted	30/03/2022 11:27
Comment	
Date Approved	04/04/2022 20:15
Approved By	Susan Dewhurst

Appendix 10. Experimental study 2 Participant Information Sheet

Bournemouth University

Participant Information Sheet

Title of research project

Does neuromuscular electrical stimulation (NMES) improve knee extensor muscle endurance in healthy older adults? A feasibility study.

Invitation to take part

You are being invited to take part in a research project. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Please take time to decide whether or not you wish to take part.

Who is organising the research?

The study is being organised by a PhD student at Bournemouth University.

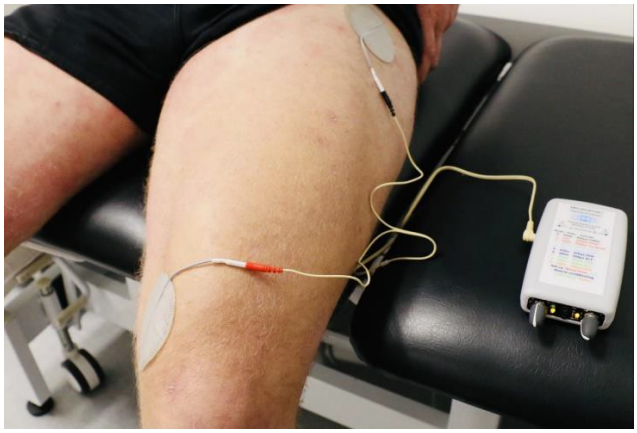
What is the purpose of the project?

To understand whether neuromuscular electrical stimulation (NMES) can increase muscle endurance of the quadriceps in healthy older adults.

What is neuromuscular electrical stimulation?

Neuromuscular electrical stimulation sends electrical impulses to nerves. This causes muscles to contract. Doing so can increase muscle strength and offset the effects of muscle disuse. It is often use to improve muscle function and to build strength before or after surgery or following a period of disuse. It's most commonly used with individuals are unable to perform voluntary exercise.

The device used in this study is a Microstim neuromuscular stimulator, made by Odstock Medical Ltd. It is the size of a mobile phone and is connected to the muscles in your leg using two self-adhesive pads called electrodes, like in the picture below.



Why have I been chosen?

You are asked to take part in this study because you are an adult aged 60 or over and in good general health. If you agree to take part, you will be one of 12 participants recruited for this study.

You will be unable to take part if you:

- Have a neurological disease affecting your walking ability (Parkinson's, cerebral palsy, multiple sclerosis, other spasticity);
- Are receiving an active medical treatment for a musculoskeletal disorder;
- Are fitted with a pacemaker or other active medical implant;
- Suffer from uncontrolled epilepsy;
- Have sepsis or osteomyelitis;
- Have a skin condition that prevents the use of self-adhesive electrodes;
- Are not able to produce an involuntary muscle contraction of the quadricep muscles using NMES (tested at your assessment);
- Are participating in any form of muscle strengthening programme aimed at improving muscle strength of endurance;
- Are unable to provide informed consent;
- Are unable to complete study follow up.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a participant agreement form. You can withdraw from participation during the study at any time and without giving a reason. If you decide to withdraw, we will usually remove any data collected about you from the study. Once the study has finished you may still be able to withdraw your data up to the point where the data is analysed and incorporated into the research findings or outputs. At this point your data will usually become anonymous, so your identity cannot be determined, and it may not be possible to identify your data within the anonymous dataset. Withdrawing your data at this point may also adversely affect the validity and integrity of the research.

What would taking part involve?

Eligible participants will be invited to attend a baseline assessment at the Orthopaedic Research Institute, Bournemouth University. Data will be collected on knee extensor strength and endurance, functional performance, daily activities and quadriceps cross-sectional area. You will be shown the NMES device and instructed how to operate it. You will then complete six weeks of NMES training at home. You will be contacted by telephone throughout the study, to have your treatment reviewed. You will be asked to record your NMES use in a diary. After 6 weeks, you will be invited to attend a final assessment where your baseline measures will be repeated. In addition, you will be asked to provide feedback on your experience of using the device.

What are the advantages and possible disadvantages or risks of taking part?

Research evidence conducted with a variety of patient groups and athletes has found that NMES can improve muscle size and strength. However very little work has been done in the area of NMES for improving muscle endurance in older adults. We anticipate NMES will increase muscle endurance, however we cannot guarantee this. You will not be paid for your participation in this study. However, we are able to send you a £20 gift card to say thank you for your time. We will also provide you with a report on your lower limb strength. There may be some discomfort from the stimulation and there is a small risk of skin irritation.

Covid-19 considerations

Personal protective equipment will be worn by the researcher collecting data. In addition, social distancing will be adhered to where possible. Face-to-face contact will be limited, and all lab equipment will undergo extensive cleaning in line with the Orthopaedic Research Institute's standard operating procedure for the decontamination of the environment and equipment during the Covid-19 pandemic. Finally, all participants will be screened for Covid-19 during their initial telephone consultation, and upon arrival at the Orthopaedic Research Institute.

What type of information will be sought from me and why is the collection of this information relevant for achieving the research project's objectives?

We will measure your weight, height and record any relevant past medical history. We will ask you to complete some strength tests using a muscle testing machine and look at the size of your quadriceps muscle using an ultrasound machine. We will also test your functional ability, which will include getting up and down from a chair, walking and climbing stairs. We will collect data on your adherence to the intervention. At your follow up appointment, we will ask for your feedback on the intervention. This data will be used to draw conclusions about the effectiveness of NMES strengthening quadriceps in healthy older adults.

How will my information be kept?

All the information we collect about you during the course of the research will be kept strictly in accordance with current data protection legislation. Research is a task that we perform in the public interest, as part of our core function as a university. Bournemouth University (BU) is a Data Controller of your information which means that we are responsible for looking after your information and using

it appropriately. BU's Research Participant Privacy Notice sets out more information about how we fulfil our responsibilities as a data controller and about your rights as an individual under the data protection legislation. We ask you to read this Notice so that you can fully understand the basis on which we will process your information.

Publication

You will not be able to be identified in any external reports or publications about the research without your specific consent. Otherwise your information will only be included in these materials in an anonymous form, i.e. you will not be identifiable. Research results will be published in an academic journal, and in the PhD thesis in which the study is a part of.

Security and access controls

Bournemouth University will hold the information we collect about you in hard copy in a secure location and on a Bournemouth University password protected secure network where held electronically. Except where it has been anonymised your personal information will be accessed and used only by appropriate, authorised individuals and when this is necessary for the purposes of the research or another purpose identified in the Privacy Notice. This may include giving access to BU staff or others responsible for monitoring and/or audit of the study, who need to ensure that the research is complying with applicable regulations.

Retention of your data

All personal data collected for the purposes of this study will be held for 5 years from the date of publication of the research or presentation of the results to the sponsor, whichever is later/ 5 year after the award of the degree. Although published research outputs are anonymised, we need to retain underlying data collected for the study in a non-anonymised form for a certain period to enable the research to be audited and/or to enable the research findings to be verified.

Contact for further information

If you have any questions or would like further information, please contact Louise Burgess (PhD student) on 01202 961651 or lburgess@bournemouth.ac.uk or Ian Swain (supervisor) on 01202 964010 or iswain@bournemouth.ac.uk.

In case of complaints

Any concerns about the study should be directed to Vanora Hundley, Faculty of Health and Social Sciences, Bournemouth University by email to researchgovernance@bournemouth.ac.uk.

Finally

If you decide to take part, you will be given a copy of the information sheet and a signed participant agreement form to keep. **Thank you for considering taking part in this research project.**

Appendix 11. Experimental study 2 – Consent form

Protocol and version: NMES in older adults, v1.0 30th March 2022
Ethics ID: 38615
Date: 04/04/22

Bournemouth University

Participant Agreement Form

Does neuromuscular electrical stimulation improve knee extensor muscle endurance in healthy older adults? A feasibility study

Name, position and contact details of researcher: Louise Burgess, Researcher and PhD candidate (01202 961651, lburgess@bournemouth.ac.uk)

Name, position and contact details of supervisor: Ian Swain, Professor in Clinical Engineering (01202 964010, iswain@bournemouth.ac.uk)

To be completed prior to data collection activity

Agreement to participate in the study

You should only agree to participate in the study if you agree with all of the statements in this table and accept that participating will involve the listed activities.

I have read and understood the Participant Information Sheet (NMES in older adults, v1.0, 30th March 2022) and have been given access to the BU Research Participant Privacy Notice which sets out how we collect and use personal information (https://www1.bournemouth.ac.uk/about/governance/access-information/data-protection-privacy).	
I have had an opportunity to ask questions.	
I understand that my participation is voluntary. I can stop participating in research activities at any time without giving a reason and I am free to decline to answer any particular question(s).	
I understand that taking part in the research will include the following activity/activities as part of the research:	
Two visits to the Orthopaedic Research Institute at Bournemouth University where data on my age, weight, height, past medical history, physical activity level, leg strength, quadriceps muscle depth and functional ability will be collected.	
Use of a neuromuscular electrical stimulation device worn at home for six weeks.	
Phone calls from the lead researcher every two weeks to review my progress.	
Feedback on the intervention I received, including adherence to the study protocol.	
I understand that, if I withdraw from the study, I will also be able to withdraw my data from further use in the study **except** where my data has been anonymised (as I cannot be identified) or it will be harmful to the project to have my data removed.	
I understand that my data may be used in an anonymised form by the research team to support other research projects in the future, including future publications, reports or presentations.	
	Initial box to agree
I consent to take part in the project on the basis set out above	

I confirm my agreement to take part in the project on the basis set out above.

Name of participant (BLOCK CAPITALS)	Date (dd/mm/yyyy)	Signature

Name of researcher (BLOCK CAPITALS)	Date (dd/mm/yyyy)	Signature

Appendix 12. NMES feedback questionnaire

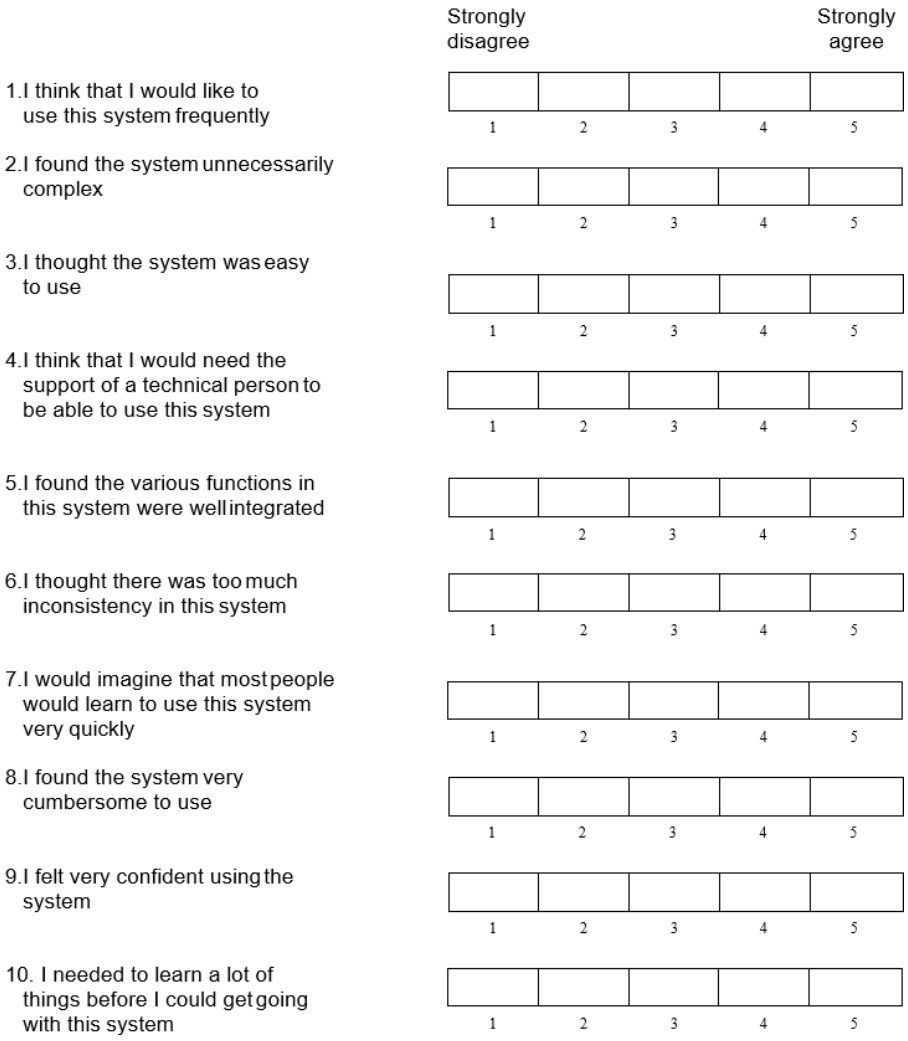
Thank you for taking part in this study to see how neuromuscular electrical stimulation (NMES) affects knee extensor endurance in healthy older adults. We are interested in finding out how you found the NMES device and would be grateful if you could complete the following questionnaire. If there are any questions you don't understand, please ask for help from the researcher collecting your data.

1. How easy did you find the NMES device to apply to your leg? (Please circle)				
Really easy	Easy	Moderate	Difficult	Really difficult
2. How comfortable did you find the NMES device to use? (Please circle)				
Really comfortable	Comfortable	Moderate	Uncomfortable	Really uncomfortable
3. Did you experience any pain during stimulation? (Please circle)				
No pain	Slight pain	Moderate pain	Considerable pain	Unbearable pain
4. Would you consider using NMES again in the future?				
Yes	Maybe	No		
5. Would you recommend using NMES to a friend who needed to strengthen their muscles?				
Yes	Maybe	No		
6. What did you like about NMES?				
7. What did you dislike about NMES?				

8. Do you have any suggestions as to how we could improve your experience of using NMES?
9. Please use the space below to let us know any other comments you may have about the NMES device or the trial:
Thank you very much for your participation in this study.

Appendix 13. System Usability Scale

System Usability Scale



Abbreviations

ASA	American Society of Anaesthiologists
AAOS	American Academy of Orthopaedic Surgeons
APTA	American Physical Therapy Association
BMI	Body mass index
CI	Confidence interval
COPD	Chronic obstructive pulmonary disorder
Covid-19	Coronavirus 2019
CRF	Case report form
CSA	Cross-sectional area
CT	Computed tomography
EMG	Electromyography
EMS	Electrical muscle stimulation
ERAS	Enhanced recovery after surgery
FES	Functional electrical stimulation
FNS	Functional neuromuscular stimulation
ICU	Intensive care unit
KNGF	Royal Dutch Society for Physical Therapy
MVC	Maximal voluntary contraction
MVIC	Maximal voluntary isometric contraction
NICE	National Institute of health and Care Excellence
NIHR	National Institute of Health Research
NHS	National Health Service
NMES	Neuromuscular electrical stimulation
OARSI	Osteoarthritis Research Society International
ORI	Orthopaedic Research Institute
PROMs	Patient Reported Outcome Measures
SMD	Standard Mean difference
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TENS	Transcutaneous electrical nerve stimulation
THR	Total hip replacement
RCT	Randomised controlled trial
WHO	World Health Organisation
WMD	Weighted mean difference
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

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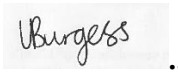
Signature of Candidate  ..... Date 06/02/2023

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Signature of Faculty Executive Dean ..... Date .....

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Document title	Lab-based feasibility and acceptability of neuromuscular electrical stimulation in hip osteoarthritis rehabilitation.
Thesis chapter	Chapter 5, section 5.4
Publication status	Published
Acceptance date	24th November 2021
Citation	Burgess, L. C., Taylor, P., Wainwright, T. W. and Swain, I. D., 2021. Lab-based feasibility and acceptability of neuromuscular electrical stimulation in hip osteoarthritis rehabilitation. J Rehabil Assist Technol Eng, 16 (8).
DOI	10.1177/2055668320980613.
Any other authors	Ian Swain (BU), Paul Taylor, Tom Wainwright (BU)
Restrict access? N (if Yes please provide details)	▪ The document and/or data contains information provided in confidence ▪ Releasing the document and/or data would cause substantial prejudice to commercial interests ▪ The document and/or data contains information about research in progress where there is an intention to publish later ▪ Other (please provide details)

Document title	Effect of neuromuscular electrical stimulation on the recovery of people with COVID-19 admitted to the intensive care unit: A narrative review.
Thesis chapter	Chapter 6 Section 6.4.3
Publication status	Published
Acceptance date	10.2340/16501977-2805
Citation	Burgess, L. C., Venugopalan, L., Badger, J., Street, T., Alon, G., Jarvis, J. C., Wainwright, T. W., Everington, T., Taylor, P. and Swain, I. D., 2021. Effect of neuromuscular electrical stimulation on the recovery of people with COVID-19 admitted to the intensive care unit: A narrative review. J Rehabil Med, 53 (3).
DOI	29th January 2021
Any other authors	Lalitha Venugopalan, James Badger, Tamsyn Street, Gad Alon, Jonathan Jarvis, Tom Wainwright (BU), Tamara Everington, Paul Taylor, Ian Swain (BU).
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Document title	Adherence to Neuromuscular Electrical Stimulation Interventions for Muscle Impairment in Hip and Knee Osteoarthritis: A Systematic Review.
Thesis chapter	Chapter 7, Section 7.4
Publication status	Published
Acceptance date	10th June 2021
Citation	Burgess, L. C., Taylor, P., Wainwright, T. W., Bahadori, S. and Swain, I. D., 2021. Adherence to Neuromuscular Electrical Stimulation Interventions for Muscle Impairment in Hip and Knee Osteoarthritis: A Systematic Review. Clin Med Insights Arthritis Musculoskelet Disord, 14.
DOI	10.1177/11795441211028746
Any other authors	Ian Swain (BU), Paul Taylor, Shay Bahadori (BU), Tom Wainwright (BU)
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Document title	Six-weeks of home-based NMES improves knee extensor endurance and function in healthy, older adults – A feasibility study.
Thesis chapter	Chapter 8
Publication status	In preparation for publication
Acceptance date	N/A
Citation	N/A
DOI	N/A
Any other authors	Ian Swain (BU), Paul Taylor, Tom Wainwright (BU)
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I request that no access of any kind be permitted to this thesis/ research data/ material in an integrated thesis (see Section B) for two years, commencing from the date of conferment. I understand that:

i. 'No access' means that no one, not even I, or my supervisor, or my Faculty Executive Dean, will have access to the deposited copy of the thesis and/or research data during this period. This restriction may, however, be lifted, for a named person for a specified period at the joint request of my Faculty Executive Dean and myself;

ii. At the end of the period, unless I make a request for the restriction to be extended, the thesis and/or research data will be made available on Bournemouth University's research and/or data repositories; a copy of the thesis will also be made available to the British Library.

iii. Restriction may be extended to a maximum of 5 years commencing from the date of conferment. The restriction then lapses and cannot be renewed. Bournemouth University Library is under no obligation to contact me about extending the period of restriction.

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	Other

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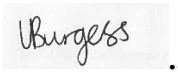
Material/data	Location within thesis	Reason for restricting access (including details of any specific restrictions agreed when the material/data was created or collected)

Signature of Candidate  ..... Date 06/02/2023

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