

BMJ Open Study protocol for neuromuscular stimulation for rehabilitation after general and vascular surgery: a pilot randomised clinical study

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To cite: Nimura M, Lane T, Rawashdeh M, *et al.* Study protocol for neuromuscular stimulation for rehabilitation after general and vascular surgery: a pilot randomised clinical study. *BMJ Open* 2023;**13**:e061800. doi:10.1136/bmjopen-2022-061800

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-061800>).

Received 11 February 2022
Accepted 27 January 2023



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ABSTRACT

Objectives To investigate the acceptability and safety of neuromuscular stimulation (NMES) as an adjunct for rehabilitation after vascular and general surgery.

Methods and analysis Prospective, single-centre, single-blind, parallel group, randomised controlled study. This study will be conducted in a single-centre, secondary care setting (National Healthcare Service Hospital) in the UK. All patients aged over 18 years undergoing vascular or general surgery with Rockwood Frailty Score of 3 or above on admission. Exclusion is inability or unwillingness to participate in trial, implanted electrical device, pregnancy and acute deep vein thrombosis. Target number of recruitment is 100. Participants will be randomly assigned to active NMES group (group A) or placebo NMES group (group B) prior to surgery. Participants will be blinded and asked to use the NMES device, 1–6 sessions daily (30 min per session) after surgery in addition to standard National Health Service rehabilitation care until discharge. The primary study outcomes are acceptability and safety of NMES assessed by the device satisfaction questionnaire on discharge and adverse events recorded during hospital stay. The secondary outcomes are the postoperative recovery and cost-effectiveness compared between two groups, assessed by various activity tests, mobility and independence measures and questionnaires.

Ethics and dissemination Ethical approvals were provided by London-Harrow Research Ethics Committee (REC) and the Health Research Authority (HRA), Ref: 21/PR/0250. Findings will be published in a peer-reviewed journal and presented at national and international conferences.

Trial registration number NCT04784962.

INTRODUCTION

Rehabilitation after surgery is an important component of the holistic care of patients undergoing surgical intervention. Increasing life expectancy is resulting in an ageing population with a greater number of comorbidities and reduced physiological reserve.^{1 2} Older people are also more likely to suffer from sarcopenia, which impacts their ability to rehabilitate postoperatively.³ This population

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Acceptability and safety of neuromuscular stimulation (NMES) after vascular and general surgery will be assessed in randomised controlled trial.
- ⇒ The postoperative recovery and cost-effectiveness will be compared between the active NMES and sham NMES groups.
- ⇒ This study only analyses the effects of NMES during the inpatient stay and does not evaluate the long-term benefits of NMES.
- ⇒ This study is not double blinded as the different instructions will be required for each group.

increase in clinical frailty undergoing surgical intervention leads to a greater demand for multidisciplinary postoperative care.

National Vascular Registry reported that length of stay (LOS) after elective vascular surgery is a median of 7 days, whereas emergency cases can be up to 22 days.⁴ National Health Service (NHS) general ward bed costs are significant, with an estimated cost of £586.59 per day,⁵ compounded by a considerable deficit in rehabilitation beds. Patients who have previously espoused that their primary desire postoperatively is for a rapid return home.⁶

Current best practice for recovery after surgical intervention is intensive physiotherapy and occupational therapy based rehabilitation to return patients to a pre-morbid independence level.⁷ However, due to patient fatigue and resource constraints, especially outside of the working week, such rehabilitation is necessarily limited to 1–2 hours of intervention per day, Monday to Friday.⁸ This prolongs inpatient stay, increases costs and delays return to home, which is often the most important outcome to patients. Increased frailty is thought to lead to increased duration of recovery to baseline.

Neuromuscular stimulation (NMES) has been shown to be beneficial in improving symptoms in claudication and venous disease and is the subject of a multicentre National Institute for Health Research randomised study.^{9–11} It has also been shown to be beneficial in accelerating recovery after orthopaedic surgery, stroke and intensive care stay.^{12–14}

NMES uses electrical impulses to cause involuntary contraction of lower limb muscle groups. This allows for continued safe muscle training without the need for therapists. These devices often use pre-set 30 min sessions, which can be repeated up to six times a day. They have been shown to be safe in multiple situations and offer a reusable and low-cost option for adjunctive intervention.^{12–14}

The aim of this study is to investigate the acceptability and safety of NMES as an adjunct for rehabilitation after vascular and general surgery and monitor the effects of NMES in postoperative recovery in terms of activity, frailty, independence and quality of life (QoL) levels.

METHODS AND ANALYSIS

Trial design

This is a single-centre, prospective single blind randomised controlled trial.

Study setting

Eligible participants will be recruited from St Mary's Hospital and Charing Cross Hospital (Imperial College London NHS Healthcare Trust, UK).

Eligibility criteria

Inclusion criteria are: medically stable after index surgery as defined by the clinical team, willing and able to participate in the study, all ethnic groups, male or female above the age of 18 years and hospital admission Rockwood Frailty Score¹⁵ of 3 or greater as defined by the clinical team. Exclusion criteria include: inability or unwillingness to participate in trial, implanted electrical device such as pacemaker or defibrillator, pregnancy (a urine pregnancy test will be performed in women of childbearing potential on admission) and acute deep vein thrombosis. Patients had previously used NMES will also be excluded.

Interventions

All eligible patients will be informed about the study and provided with a written information sheet. After gaining consent, baseline demographic data, including medical history and any concomitant medication will be collected for each participant. EuroQol Five-Dimensions 5 Level Domain Utility Index+Visual Analogue Scale (EQ5D5L+VAS)¹⁶ and 36-Item Short Form Survey (SF-36)¹⁷ will also be completed as baseline assessment. The patients will then be randomly allocated to either the intervention group (group A) or the placebo group (group B) (figure 1).

Participants in both groups will be blinded and asked to use the device 1–6 sessions daily (30 min per session) after surgery in addition to standard NHS rehabilitation care with occupational therapists, physiotherapists and rehabilitation physicians. Device instruction will be given by trained registered healthcare professionals on the first assessment (when medically stable post operatively as defined by the clinical team). Participants will be asked to use the device until discharge. The investigators were not blinded to the allocation as the different device instructions will be given to each group. Participants in group B will be asked to select intensity 25, not to adjust the intensity.

Patient and public involvement

No patient involved as this is a pilot study and it is designed to assess the feasibility and acceptability of the study and intervention.

NMES device

The device investigated (REVITIVE Medic, Actegy Health) is a class IIa medical device, CE marked for in treating disorders of the lower limb (figure 2). The device is used in the seated position, with the users' bare feet placed on a pair of conductive footplate electrodes (figure 3). Electrical impulses are delivered to the muscles and nerves of the feet, which cause foot and calf muscle contraction. Direct contact between skin and electrodes is required for stimulation, precluding the use of compression stockings. Both feet have to be placed on the conductive footplates for the device to work. Although infrequent, potential side effects of NMES include skin irritation and muscle pain.

The device runs a 30 min programme of NMES consisting of 15 different waveform patterns, each with varying electrical output characteristics. The intensity of stimulation ranges from 1 to 99 units, delivering a maximum current of 15 mA (r.m.s., root mean square) at 500 Ω resistance. Pulse duration will be 450–970 μ s and pulse frequency will be 20–53 Hz. Stimulation intensity will be increased by the subject until visible calf muscle contraction is seen (group A). Patients will be advised to use the highest intensity that was comfortable for them. The intensity of stimulation varies for each individual and is affected by oedema and moisture. The sham device looks identical to the active device, but no effective electrical impulses are delivered to contract the muscles. Participants in group B will be asked to select intensity 25. All participants will be asked to fill in the usage diary (patient diary). The diary will be collected on the day of discharge. REVITIVE Medic was used in this study for its ease of use and commercial availability. The device manufacturer has agreed to supply the active and sham investigational devices free of charge. Patients in both active and sham groups will be allowed to keep the device at the end of their participation. Participants in the placebo group will be offered a free active device after their participation.

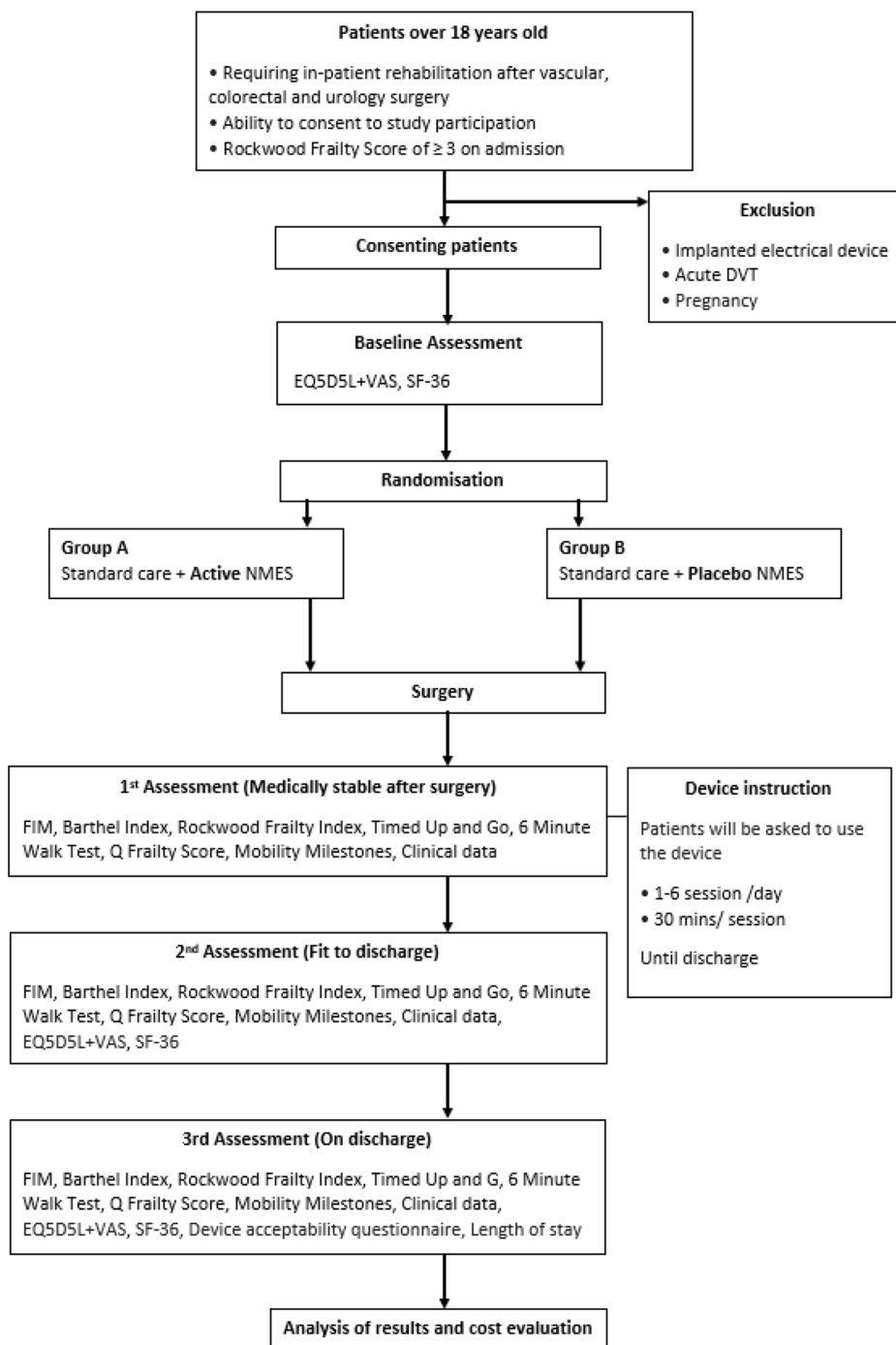


Figure 1 Trial flow chart. DVT, deep vein thrombosis; EQ5D5L+VAS, EuroQol Five-Dimensions 5 Level+Visual Analogue Scale; FIM, Functional Independence Measure; NMES, neuromuscular stimulation; SF-36, 36 Item Short Form Survey.

Assessment points

Base assessment: On recruitment.

First assessment: Once medically stable following operation as defined by clinical team.

Second assessment: When medically fit for discharge as defined by clinical team.

Third assessment: On the day of discharge from hospital.

Primary outcome

The primary outcome of this study is acceptability and safety of NMES as an adjunct for rehabilitation, assessed

by semistructured questionnaire and medical record on discharge.

Secondary outcomes

The secondary outcomes are to compare the two groups with respect to:

- ▶ Time to return to baseline mobility and independence on third assessment.
- ▶ Generic QoL-SF-36 and EQ-5D-5L QoL and VAS on base, second and third assessment.
- ▶ Functional Independence Measure¹⁸ on 1st–3rd assessment.



Figure 2 NMES device, 2022, Actegy. NMES, neuromuscular stimulation.

- ▶ Barthel Index¹⁹ on 1st–3rd assessment.
- ▶ Rockwood Frailty Index¹⁵ on base, 1st–3rd assessment.
- ▶ Timed Up and Go Test²⁰ on 1st–3rd assessment.
- ▶ 6 min Walk Test²¹ on 1st–3rd assessment.
- ▶ Satisfaction with device on third assessment.
- ▶ Compliance with device usage on third assessment.



Figure 3 Device application, 2022, Actegy.

- ▶ Length of hospital stay on third assessment.
- ▶ Q Frailty Index Score²² on 1st–3rd assessment.
- ▶ Mobility Milestones on 1st–3rd assessment (yes/no assessment).
 - Sitting for >5 min.
 - Standing for >1 min.
 - Walking >50 m (50 m will be measured and marked in ward by the research team using a measuring wheel).
- ▶ Hospital resource use (patient diary and clinical record) on third assessment.
 - Contacts with rehabilitation professionals.
 - Contacts with healthcare professionals during NMES sessions.
- ▶ Incremental cost–utility ratio, comparing NMES with standard care during the hospital admission on third assessment.

Assessments will be conducted by trained registered healthcare professionals (physicians or nurses).

Study feasibility

Feasibility of recruitment will be assessed by: number of participants referred, number of participants eligible for screening, number of participants enrolled, reasons for non-participation will be captured.

Feasibility of measurement tools will be reviewed by: time taken to complete the questionnaires at each timepoint, missing data from questionnaires, follow-up response rates.

Adherence is assessed by: number of times the NMES device used and time spent using the NMES device.

Sample size

As a pilot study, no formal power and sample size calculation have been completed. However, a pragmatic study to assess acceptability and early trends has been planned. This requires 100 patients—50 in each group.

Utilising early inpatient local data (n=40), a reduction in the mean LOS from 22 to 20 would require 2400 patients, however, it is anticipated that this study will generate data to inform a more accurate baseline to power a large multisite study, if NMES is found to be acceptable.

Study duration

Study setup is expected to take 3 months. Target recruitment is anticipated to take 12 months. This consists of nine patients per month. Follow-up of patients is until discharge, which is estimated to be up to 1 month. Study close-down, data analysis and manuscript preparation are expected to take 2 months. The end of study will be the date of last data collection of the last participant.

Recruitment

Potential participants will be identified at preadmission clinic appointments and operation lists. Posters and leaflets will be displayed in clinics, wards and other appropriate locations.

Potentially eligible patients will receive a verbal explanation of the study and a patient information sheet by the attending research team.

Randomisation schedule

Patients will be allocated randomly to one of the two groups by equal randomisation, using an online computerised randomisation system (SealedEnvelope, London, UK).

Blinding

Participants will be blinded to group allocation. Participants in group B will be asked to use intensity 25.

Statistical analysis

Data will be analysed using SPSS V.24 (IBM) STATA V.15SE (StataCorp) or a similar statistical software. Data will be analysed on an intention-to-treat basis. Visual testing and Shapiro-Wilk testing will be performed to assess the distribution of the data. For continuous data, if the data are normally distributed mean and SD will be presented, whereas median and IQR will be presented if it is not normally distributed. For categorical data, frequencies and percentages will be presented. T-tests may be conducted if the data are normally distributed, whereas the Mann-Whitney U test may be more desirable if the data are not normally distributed. A repeated measure analysis of variance will be used to examine changes in scores from baseline during follow-up. All time-to-event outcomes will be assessed using Kaplan-Meier curves and log-rank tests for group comparison. χ^2 tests will be performed to compare treatment group proportions. Missing data will be handled with multiple imputation methods.

Cost-effectiveness analysis

Cost-effectiveness analysis for both groups will be assessed using the cost of the equipment and hospital stay, the cost of personnel involved and QoL gain following the patient stay.

The number and timing of sessions with physiotherapists, occupational therapists and rehabilitation physicians in both groups will be collected using patient diaries during the hospital stay. Costs will be estimated using manufacturer's list prices and national reference costs. QoL gain will be estimated using the EQ-5D instrument. The incremental cost-per-quality-adjusted life year (QALY) will be calculated. The extent of any missing data will be examined and appropriate analytical methods used. Sensitivity analyses will explore any factors that substantially change the mean cost per QALY. Discounting will not be applied as the time horizon is less than 1 year. The price year will be 2020/2021. The health economic analysis will be conducted from the perspective of the UK NHS according to standard methods guidelines.

Data collection and confidentiality

Patient records will be made on paper forms and stored in a locked cabinet in a locked research office at Imperial

College London. All pseudonymised participants data with the allocated study number used as identifier will be stored electronically on a password-protected access database on an Imperial College London university computer under the guidelines of the Data Protection Act 2018 and General Data Protection Regulation. Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

Data monitoring, safety and quality control

All adverse events (AEs) and severe AEs (SAEs), whether related to the intervention or not should be recorded. SAEs should be notified to the chief investigator (CI) within 24 hours. All SAEs should be reported to the research ethical Committee where, in the opinion of the CI, the event was related or unexpected. Reports of related and unexpected SAEs should be submitted within 15 days by the CI, using the National Research Ethics Service SAE form for non-investigational medicinal product studies. Local investigators should report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research and Development Office.

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study. The study will be monitored and audited according to the policies of the Joint Research Compliance Office of Imperial College London.

Limitations

Possible limitations of this study are: (1) Single blind study. The investigators will not be blinded as the different instructions need to be given to each group. (2) This study will only investigate the effects of NMES during hospital stay and not evaluate the long-term effects of the device. The duration of NMES treatment depends on the length of hospital stay. (3) Ability to blind participants. The participants may realise their allocation due to activity/inactivity of the device.

DISCUSSION

Current postoperative rehabilitation is limited due to resource constraints. NMES is safe, low cost and can be used without supervision. When the conventional postoperative management is restricted by staff shortages, and for the patients who unable to participate in the exercise therapies, NMES may be an effective alternative. This study is to investigate the acceptability and safety of NMES as an adjunct for rehabilitation after vascular and general surgery.

ETHICS AND DISSEMINATION

Ethical approvals were provided by London-Harrow Research Ethics Committee (REC) and the Health Research Authority (HRA), Ref: 21/PR/0250. Findings

will be published in a peer-reviewed journal and presented at national and international conferences.

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Acknowledgements The authors wish to thank the clinical, nursing and physiotherapy teams in Colorectal, Urology and Vascular surgery at Imperial College Healthcare NHS Trust.

Contributors All authors (MN, TL, MR, SO, AJ, GS, GR, DH and AHD) drafted the study protocol and design. TL, SO and AHD participated in designing the study and securing funding. TL and MN coordinate the project and drafted the manuscript. MN recruits and obtains consent from the patients. MR, AJ and TL will perform the statistical analysis. AHD supervises the project. All authors have read and approved the final manuscript.

Funding This study is supported by the Jon Moulton Charity Trust and Imperial College London. Grant number not available. NMES device will be provided free of charge by Actegy Health.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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