Appendix S1

East Kent Hospital University Foundation Trust and Rex Bionics		Document Number **0001-P**
TITLE **REX ROBOT ASSISTED REHABILITATION EXERCISE TO ENHANCE BALANCE, MOBILITY AND UPPER LIMB FUNCTION IN PEOPLE WITH MULTIPLE SCLEROSIS "RAPPER III – MS**	REVISION NUMBER 1	EFFECTIVE DATE 29/09/2016

Rex robot Assisted rehabilitation exercise to enhance balance, mobility and uPPER limb function in people with Multiple Sclerosis "RAPPER III – MS"

Proposed Study Synopsis

Title	Prospective, open label, single arm, non-randomized, non-comparative feasibility study of Rex robot assisted rehabilitation exercise to enhance balance, mobility and upper limb function in people with Multiple Sclerosis "RAPPER III – MS
Objective	The objective of this study is to evaluate the feasibility and safety of the REX Robot when used for rehabilitation with people who have moderate to severe mobility restrictions due to MS. A secondary objective of the study is to explore the acceptability of the device to people with MS and its impact on impairments and functions commonly affected by MS.
Study Sponsor	Rex Bionics, Plc.
Study Device	REX Robotic powered exercise system
Primary Endpoint	• Completion of a transfer, stand, balance and walk rehabilitation session. • Unexpected Serious Adverse Events
Secondary Endpoints	• Completion of a transfer, stand, balance and walk rehabilitation program over Six-weeks • The Number of approached, screened, and eligible potential participants. Reasons for Ineligibility. (See 'RAPPER III- MS 007 Screening Loss Analysis REV 0 FINAL') • Functional Ambulation Classification (FAC) [1] • Activities-specific Balance Confidence (ABC) Scale [2] • Modified Falls Efficacy Scale (MFES) [3, 4,] • Multiple Sclerosis Walking scale (MSWS-12) [5] • Multiple Sclerosis Impact scale (MSIS-29) [6] • ARMA (arm activity measure) [7]

	• Berg Balance Scale [8] • Timed unsupported steady stand (TUSS) [9] • Pain scale questionnaire (Visual Analog Score VAS) [10] • Modified Ashworth Score [11] • Spasticity Impact Scale [12] • Epworth Sleepiness Scale (ESS) questionnaire [13] • EQ-5D Health State Questionnaire [14] **Questionnaires may be administered in person, by phone, email or in the post.**

Study Design	This feasibility study is an Open Label, Non-Randomized, Non-Comparative, Open Registry Study. The intent is to evaluate the feasibility and safety of using the Rex Robot in rehabilitation with people with MS who have moderate to severe mobility restriction. Therefore, this feasibility study will include a group of ten people aged between 18 and 90 years who have a primary diagnosis of MS, with an EDSS score of between 6 and 7.5. Following screening by a medical professional and the provision of informed consent, eligible participants will undertake a baseline assessments of Health Reported Quality of Life (HRQoL)/participation, function, and impairment using standardised outcome measures. They will then participate in a six-week rehabilitation intervention. The intervention will include a once weekly Rex Robot assisted physiotherapy exercise programme under the supervision of a trained neuro physiotherapist. The aim of the programme is to increase strength, improve balance related skills and walking ability. Response to the intervention will be monitored based on reporting adverse events, negative symptoms and pain. Following the intervention period, the outcomes of HRQoL/participation, activity, and impairment will be re-evaluated. In addition, the Psychosocial Impact of Assisted Device Scale (PAIDS) [29] will be used at the end of the program to investigate device acceptability. The safety of the intervention will be evaluated based on reported adverse events and negative symptoms.
Exercise programme Intervention	This will be taught and supervised by the Rex-trained Specialist Neuro-physiotherapist of the research team. This neuro-physiotherapist will have direct access to the Principal Investigator (PI), Consultant Neuro-rehabilitation Physician and Physiotherapy Specialist from the Industry Sponsor, who has experience of use of this device with other patients. **The Exercise Programme Intervention:**

	Please refer to the "Treatment Intervention Manual" (See 'RAPPER III- MS 005 Treatment Intervention Manual REV 0 FINAL 2') for guidance on the treatment intervention required for session 1-6.
Number of participants	The total number of enrolled participants will be 10. As a feasibility study this study is not powered to detect a statistically significant intervention effect.
Stopping Rule	• Any unexpected serious adverse events (life threatening or requiring medical intervention due to the use of the device) • Any participant death as a result of use of the device
Duration of study	Each eligible participant will have: 1. Initial baseline assessment followed by pre-treatment outcome measures being taken. Followed by a videoed sit to stand, stand to sit and a Timed Up and Go test (TUG) [28] to be done outside of the device. This will be followed by a timed transfer into the device. 2. A course of 4 exercise sessions will take place after the initial assessment. Each a week apart. After the 2nd exercise session, outcome measures will be taken on spasticity, pain and sleep using: Pain scale questionnaire (Visual Analog Score VAS); Modified Ashworth Score [11]; Spasticity Impact Scale [12]; Epworth Sleepiness Scale (ESS) questionnaire [13] 3. Final baseline assessment will be done in session 6 when all clinical measures are repeated. Thus the total number of visits would be 6 per participants over a time period of 6 weeks (approximately 1 visit per week). The total duration of the participants' commitment to the study is 7 weeks (including screening time). The total time commitment for a participant will be between 7.5 hours (excluding travel) dependent on the time taken to complete screening, baseline and post-intervention assessments. It is estimated that screening and baseline assessment will take approximately 180 minutes (a substantial proportion of this will be self-reported and done from home), each intervention session will last for 45 minutes (4 sessions x 45 = 180 minutes) and the post-intervention assessment will take up to 90 minutes (a substantial proportion of this will be self-reported and done from home). Based on the above estimates the total duration of the study including data analysis and write up is expected to be 38 weeks.

Inclusion/Exclusion criteria	Participants are considered eligible for enrolment in the trial if they fulfil all of the following criteria: ***Inclusion Criteria:*** Individuals will be considered eligible for enrolment in the study if they fulfil all of the following criteria: • Are aged greater than 18 years and less than 90 years • Have a confirmed diagnosis of MS by a Consultant Neurologist as per Mc Donald Criteria. • Have moderate to severe mobility restriction as defined by an Extended Disability Status Scale (EDSS) score of between 6 to 7.5 (inclusive). • Meet the anthropometric requirements of the REX device (See 'RAPPER III-MS 014 TF-04 v 3.0 REX Clinical Assessment Guide A4' for details of weight, height, size and range of motion requirements) • Offer written informed consent to take part in the study ***Exclusion Criteria:*** Individuals will be excluded from the study if they have any of the following: • a history of osteoporosis or osteoporosis related bone fractures. • skin integrity issues that could be adversely affected by the REX device • severe hypertonia (spasticity) as indicated by a score equal to or greater than 4 on the modified Ashworth scale on any muscle in their lower limbs. • a behavioural, cognitive or communication impairment which could interfere with the ability to participate in a rehabilitation programme, as noted during screening (e.g., agitation, inability to follow two step commands) • Are unable or unwilling to provide informed consent • Are considered medically unsuitable for rehabilitation in the opinion of the screening medical specialist • a known allergy (skin contact) to materials used in Rex • Are pregnant
Treatment schedule	See 'RAPPER III- MS 004 Study Schema Rev 0 FINAL'
Study	Consented participants will have the following screening / baseline assessments

procedures - baseline	performed prior to enrolment: Prior to being permitted to enter the trial and undertaking the exercise programme: • Review of medical history and medications. • Review of cardiac function – if there is any history of impaired cardiac function, or any current signs showing cardiac impairment, it is at this point the subject should be referred to a medical professional for further evaluation to determine whether they should be included or excluded from the trial. • Assessment of skin integrity All assessments will be performed by the study site's REX trained health care professional. If the health care professional is in any doubt over a user's medical history, they should be referred to a medical professional for a review and clearance to continue in the trial. If there is a history of orthostatic hypotension or impaired cardiac function they should be referred to a medical professional for further investigation prior to inclusion in the trial. The investigator will confirm, with a signed CRF, the participants eligibility after all baseline tests, and if required, laboratory results, have been reviewed. Participants not meeting enrolment criteria will not be considered for study procedures. The medical reason or other for why they were not enrolled will be recorded and a screening loss analysis will take place at the end of the study. (See 'RAPPER III- MS 007 Screening Loss Analysis REV 0 FINAL')
Study procedures:	***Refer to the "RAPPER III- MS 005 Treatment Intervention Manual REV 0 FINAL" for all tasks to be completed in each session*** **Recruitment**: Participants will be recruited to the study from the chief investigators clinics and inpatient wards at East Kent University Hospital Foundation Trust. Flyers (See 'RAPPER III- MS 010 Trial Flyer REV 0 FINAL') will be sent out to patients through GP's, Consultants and MS Specialist Nurses to invite them to take part in the study. Advertisement at the Kent MS therapy centre. A flyer in the MS news magazine. The study will also be discussed at the regional brain injury conference in Canterbury. Potential participants recruited will be identified by staff at these organisations and handed or posted a Patient Information Sheet (PIS) (See 'RAPPER III- MS 003 Patient Information sheet Rev 0 FINAL') Those interested in participating will then either contact the research team or give permission for the organisation to give their details to the research team so they can be contacted. Potential participants

who respond via local media advertising will contact the study team independently and will be given an PIS and offered the opportunity to have the study verbally explained to them and ask questions. The number of people approached to consider participation in the study will be recorded.

Screening: Potential participants who are interested in taking part in the study will be asked to give informed consent after reviewing the information sheet and screened for eligibility against the study inclusion and exclusion criteria by the Study PI (principle investigator) and Co-investigators. This screening process will involve either a face to face meeting or a telephone call to go through the screening document (See 'RAPPER III- MS 006 Enrollment Screening REV 0 FINAL') with the study PI or investigators. The potential participant will also have the opportunity to have the study verbally explained and ask any questions.

Baseline Assessment (session 1): Following screening, potential participants will be offered an appointment time for baseline assessment. All assessments will be individually administered according to standardised procedures by a trained research physiotherapist. Demographic characteristics of participants including age, sex, ethnicity, clinical characteristics of their MS, medical history, current medications and precautions and contra-indications to mobility, exercise and device use will be gathered. A detailed assessment for fit in the REX device will be undertaken this includes evaluation of the participant's anthropometric measures to ensure safe device use in accordance with REX bionics requirements (See 'RAPPER III- MS 014 TF-04 v 3.0 REX Clinical Assessment Guide A4') Outcome measures of impairment, activity and HRQoL/Participation will be conducted.

The investigator will confirm, with a signed CRF, the participants eligibility after all baseline tests, and if required, laboratory results, have been reviewed.

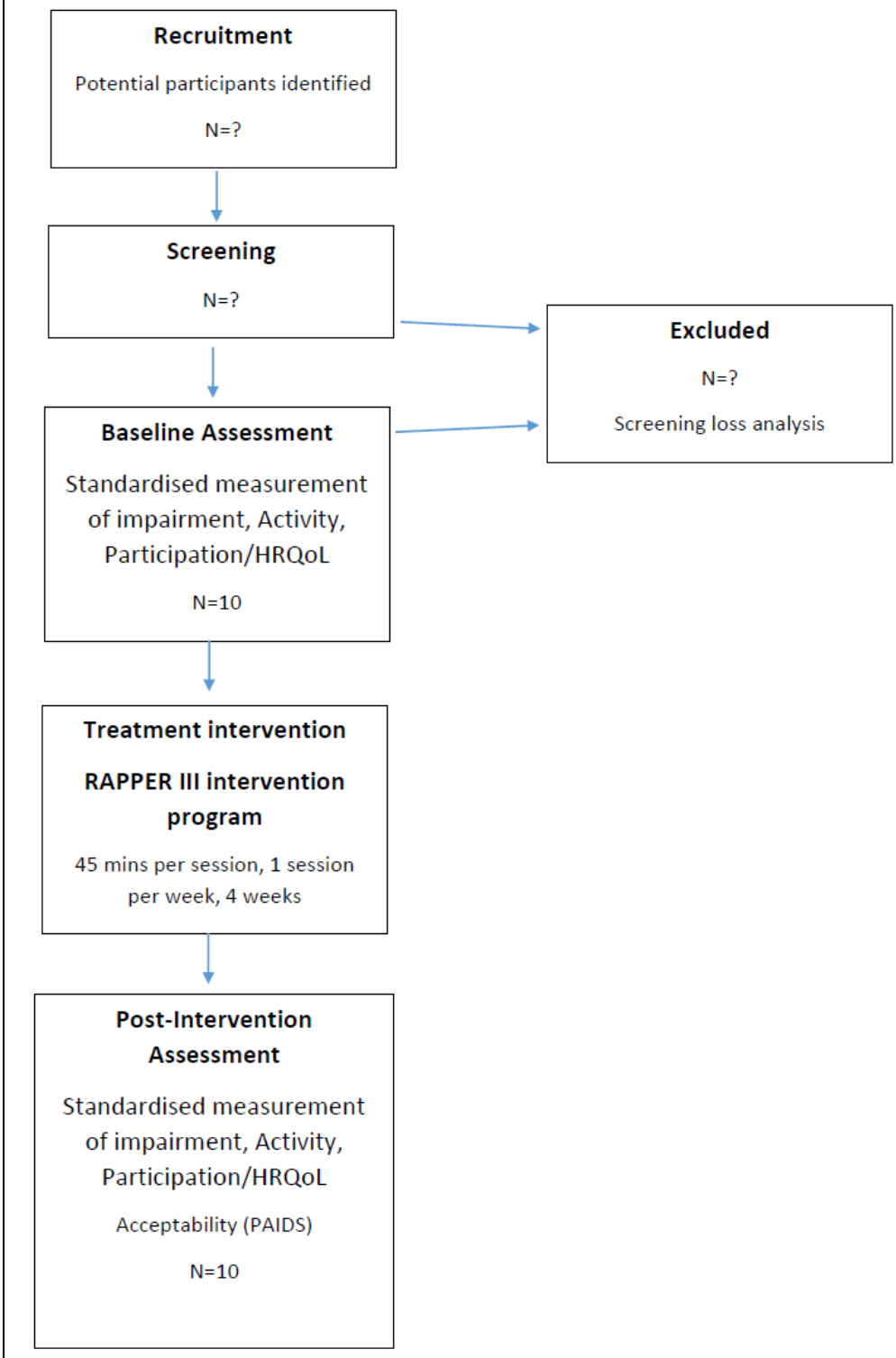
Intervention (session 2-5): Participants will participate in a four week, once per week rehabilitation programme as described in the "Treatment Intervention Manual" (See 'RAPPER III- MS 005 Treatment Intervention Manual REV 0 FINAL') Any adverse events will be recorded with the "adverse event form" (See 'RAPPER III- MS 008 Adverse Event Form REV 0 FINAL') After session 3 and 5 participants will be assessed against the following:

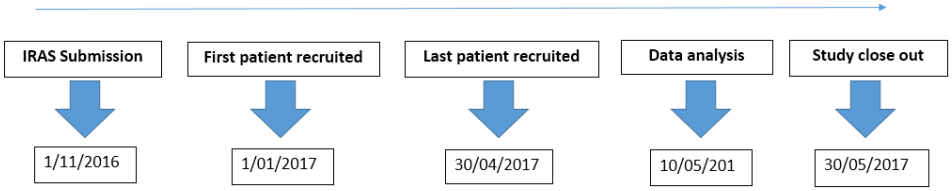
- Pain scale questionnaire (Visual Analog Score VAS);
- Modified Ashworth Score [11];
- Spasticity Impact Scale [12];
- Epworth Sleepiness Scale (ESS) questionnaire

Post-Intervention Assessment (session 6): In the week following the end of the intervention phase all outcome measures conducted in the baseline assessment

	will be re-administered according to the same standardised procedures as described in the Baseline Assessment. Post-intervention evaluation of device acceptability will be evaluated using the Psychosocial Impact of Assisted Device Scale (PAIDS). [29]

Study Flow chart



Time Line	
Follow-up and Safety	**Intervention monitoring** After each session the research physiotherapist will assess the participants to identify any adverse events or negative symptoms including skin redness or abrasion, swelling or pain. If there are any negative symptoms this will be followed up with a phone assessment 24 hours later to identify if the issue has resolved. If it has not, then a follow up assessment in the clinic with the Chief investigator (Dr Sakel) will need to be scheduled if deemed necessary **Adverse Event reporting** Adverse events are defined as an event which caused the participant to seek attention from a health professional, or limited their activities of daily living for at least two days. A serious adverse event is defined as "Any adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect." In the event of an identified or participants reported adverse event the research physiotherapists is required to complete an adverse events form (See 'RAPPER III- MS 008 Adverse Event Form REV 0 FINAL') which includes participant details, a description of the event, its outcome, details of any medical care required and any relationship between the adverse event and the rehabilitation programme. The form is then passed onto the study PI for review. Any adverse events will be reported to the local ethics committee in accordance with their procedures.
Statistical considerations	The Principal Investigator received advice from the Statistician employed by the R & D Directorate of the East Kent University NHS Hospital who will be consulted once the study is completed. Descriptive statistics will be presented for all endpoints, primary and secondary.

	Comparisons to mean values, where applicable will be presented. Since, this is a pilot study on a novel group of participants (people with MS), statistical significance is not the target objective. The aim of the study is to ascertain whether the intervention is safe and can improve some specific functionalities of such a patients cohort. All functionalities of all 10 participants will be compared before and after the intervention period and presented in graphics to demonstrate any changes and the time taken for that benefit to accrue. This will then inform to calculate the sample size for a larger RCT in future. Data will be analysed for the study populations according to the following definitions: ***Intention-To-Treat Analysis (ITT):*** The Intention-To-Treat (ITT) population will be defined as all participants enrolled in the trial whether or not they received treatment. ***Per-Protocol Analysis (PP):*** The Per-Protocol (PP) population will include all ITT patients excluding participants with major protocol deviations or early withdrawals. ***Sub Group Analyses (SG1)*** A Sub Group analysis will be presented of study subjects to assess any differences in outcomes of balance, spasticity and sleep. P- Values will be identified where appropriate. No Interim Safety Analyses will be performed.
Administrative information	Principal Investigator: Dr Mohamed Sakel. MRCP. FRCP. Consultant Physician in Neuro-rehabilitation. East Kent Hospitals University NHS Foundation Trust (EKHUFT). **Total number of study sites:** 1-3

Protocol Title: Rex robot Assisted rehabilitation exercise to enhance balance, mobility and uPPER limb function in people with Multiple Sclerosis "RAPPER III – MS"

Principal Investigator:
Dr Mohamed Sakel, Director / Consultant Neuro-rehabilitation Physician

Co-Investigators:
Dr Matthew Pepper
Karen Saunders
Layla Larsen
David Stevenson
Thomas Priestley

Project sites: LEAD SITE - East Kent Hospitals University NHS Foundation Trust (EKHUFT).

Sponsor: Rex Bionics PLC

Background:

Multiple Sclerosis (MS) is a chronic inflammatory- demyelinating disease of the central nervous system leading to progressive impairment of various CNS systems. [15]

Multiple sclerosis (MS) is diagnosed in 3.5 to 6.6 people per 100,000 of the population each year, equivalent to about 1,800 to 3,400 people year in England and Wales. Prevalence is between 100 to 120 per 100,000 of the population, equivalent to about 52,000 to 62,000 people with MS in total in England and Wales. Some people with MS develop few symptoms, but for others the disease and society's interactions with them lead to problems affecting all aspects of their lives. The disease often has an impact upon the family. NICE Guidelines recommend all patients with MS should have access to specialist Neurorehabilitation services. [16]

Balance and Mobility:

Millions of people around the world suffer from mobility impairments; in 2012 it was estimated that around 6.5 million people in the UK alone live with reduced mobility. [17] Balance is often compromised by the inflammatory process with multiple sclerosis and such impairment can impact on motor and sensory nerve pathways causing reduced muscle power, co-ordination, walking and functional abilities.

The ability to walk and negotiate the environment independently is fundamental to all aspects of daily life and almost all aspects of social participation are dependent upon adequate mobility. Limitation in mobility is one of the prime determinants of the amount (time and number of people) of 'care needs', whether given by family or paid carers.[16] Limitation in mobility is common in people with MS. For example, in one study 58% of people could not climb stairs unaided and 42% needed mobility aids including wheelchairs.[16] The construct of mobility is or can be much broader than simply walking. It includes moving in bed, getting out of bed, moving into and out of chairs, going up and down stairs and slopes, getting to and from shops, using special mobility equipment such as walking aids and wheelchairs, and using public transport. It may also include endurance. Reduced mobility is a common disability in many neurological and non-neurological conditions, and many studies have investigated treatments focused on improving mobility, usually walking. Furthermore, improvements in (or reduction in loss of) mobility are a common outcome measure in many other studies, including almost all interferon beta trials (the EDSS is primarily a measure of mobility). [16]

Two RCTs and one randomised crossover trial assessed different interventions for mobility problems (Ib). The first RCT examined the use of fully trained service dogs for wheelchair mobile people with MS. [18] The results showed significant beneficial effects on all of the eight outcome measures assessed including psychological, social, employment and care needs indices. The second RCT assessed the intervention of awareness through movement classes compared to just educational sessions. The results showed no difference in the number of falls or functional balance performance or self-efficacy between the groups. [19] The randomised crossover trial compared hospital outpatient physiotherapy to home-based physiotherapy and no treatment. The results showed beneficial effects for the majority of outcomes assessed for physiotherapy interventions. There were no overall differences observed between the different physiotherapy interventions. [20]

It is estimated that 15 years after disease onset 15% of MS patients need technical aids for walking and 29% use a wheelchair. [21] The reduction in mobility stems from various factors including weakness of muscles, spasticity, impaired balance, falls, fear of falls. Interventions that have potential to improve mobility include botulinum toxin therapy for multi-focal spasticity, Functional Electric Stimulation (FES), fampridine (4-aminopyridine) and multi-disciplinary physiotherapy support with or without partial body weight supported Treadmill exercise.

Robotics:

We recently completed a study using Rex Bionic robotic exo-skeleton device for people with injury at the level of spinal cord due to trauma, MS or any other cause. (NIHR Portfolio study INJU 4519) Manuscript under review). That study showed safety of the device and user friendliness of the device. There are anecdotal qualitative commentary of patients about the ease and usefulness of that assisted mobility.

http://www.itv.com/news/meridian/update/2016-04-11/one-small-step-pioneering-robot-technology-helps-patients-find-their-feet/

https://www.crn.nihr.ac.uk/monthly-insight/robotic-physiotherapy-could-prevent-further-medical-conditions-in-patients-with-reduced-mobility/

Anecdotal comments from patients and their GP include:

"Brilliant to stand upright again"

"slept well that night and 1 week after the exercise with this robot"

1. Benefits of This Study:

MS is a life-long condition, which impacts significantly on quality of life and functional abilities. These inabilities may be linked to balance and mobility impairments caused by the disease. Some abilities to perform activities of daily living (ADL) may be affected despite an individual having no significant upper limb or trunk impairments. Due to a lack of mobility, patients' upper limbs and trunk can become weak, and this can further contribute to a lack of confidence and the development of a fear of falls. Neuro-rehabilitation of these patients would include strengthening of the upper limbs and trunk muscles in an upright position in order to optimise postural muscle activation against gravity, along with challenging balance reactions. Treatment aimed at enhancing dynamic balance systems and muscle strengthening in standing can be more easily facilitated by the use of an exo-skeleton type robotic device like the Rex Rehab, which enables hands-free assisted mobility and exercise practice. Rehabilitation programs should focus on the facilitation of individual independence and supporting optimal integration back into the individuals chosen community role and lifestyle. This requires appropriate provision of support, care and necessary specialized equipment [24]. Effective rehabilitation has a key part to play in reduced length of stay (LOS), secondary complications leading to unplanned readmissions to hospital and quality of life (QoL) [25, 26]. Often equipment is necessary to compensate for loss of muscle function experienced by people with MS. Support from external structures to splint the lower limbs and trunk is needed to enable patients to adopt the upright posture of standing against

gravity. Without such supportive equipment within a care setting, carers would have to take the majority of the strain to support the individual's rehabilitation needs. With health and social care having the highest number of reported injuries in 2013/14 out of any industry and an average of 6.6 days lost to each episode, this is something that needs addressing to help prevent injuries to carers and so reduce the costs of care. [27]

This study aims to gain an insight into the potential health benefits of using a Rex robot to assist in a neuro-rehabilitation intervention program with supervision from a specialist clinician.

2. Device Description

Overview

REX is an adjustable version of the Rex Bionics robotic walking device and is worn on the lower limbs by mobility-impaired users to provide enhanced functional mobility for exercise and rehabilitation purposes.

Figure 1: Image of REX

REX is designed for use in a clinical environment, under the supervision of trained professionals. It is sophisticated, yet simple to use and operate. REX can be easily adjusted to suit a variety of users. The user typically transfers into REX in a seated position and is supported within the device by leg braces, straps and a harness.

Once secure, the user controls REX with a 3 button keypad and joystick. REX is powered by an on-board interchangeable battery pack.

The functionality of REX enables a user to perform, within a controlled environment, the following mobility functions:

- Standing
- Sitting
- Walking on flat surfaces

- Stepping
- Turning

Intended Use

REX is intended for use in a controlled environment such as a rehabilitation center or hospital under clinical supervision.

REX is suited to persons with a physical impairment, such as with spinal injuries, who are wheelchair users. In practice, a combination of factors will ultimately determine whether a user is suited to a REX. The suitability of REX for a particular person is something which must be determined by an appropriately qualified clinician, and will be based on factors such as:

- The range of motion in the user's joints
- General wellness, including skin and bone integrity
- Height and weight as per user requirements below

REX is designed to be used on a flat, stable, dry surface, such as that which would typically be found in a physical rehabilitation environment. Using REX on unsuitable surfaces may decrease stability and lead to an increased risk of personal injury and/or damage to the device.

3. User Requirements (unless otherwise specified in inclusion/Exclusion criteria)

See 'RAPPER III- MS 014 TF-04 v 3.0 REX Clinical Assessment Guide A4'

Anticipated Results and Potential Pitfalls:

No serious adverse events are expected as the suitability of a participants to perform the prescribed exercise program is to be assessed by the participants trial neuro physiotherapist prior to entry into the study. However, any Serious, Unexpected Adverse Events will result in the study being stopped.

As in many rehabilitation processes, patients may experience discomfort or pain, which is not considered a serious adverse event.

Some participants may not be able to complete the exercise program. These will be considered failures with respect to the associated endpoints and reason will be documented.

Adverse Events

All adverse events (whether serious or not, related to the device or not) will be recorded on the Adverse Event CRF.

Adverse Event – any event of injury, extreme pain, accident or other event deemed as such by the medical practitioner or physiotherapist.

Serious adverse events – those events which may be life threatening, or require medical intervention to prevent further injury.

Unexpected Serious Adverse Events – those events which meet the criteria above, but are not listed as expected in this protocol, the User manual or Investigational brochure. All Unexpected, Serious Adverse events may be reported to the Ethics Committee or IRB, as well as the appropriate national health Authority as required by the health care institution or the country specific regulations.

MS Charity support:

Principal Investigator has discussed with Kent MS Therapy Centre (KMSTC) about the planned research. The Trustee Board member and Manager of the KMSTC provided enthusiastic support after watching the narrative in local TV and MS News Magazine. They encouraged one of their patients to participate in our previous study on spinal injury due to MS. That participants good experience motivated this charity to support this planned study exclusively for MS patients. They have also pledged to support recruitment by promoting the study in their centre.

Ethics

This study will be conducted, evaluated and documented in accordance with the ethical principles that have their origin in the Declaration of Helsinki (59th WMA General Assembly, Seoul, October 2008) consistent with GCP as required by the most current ICH Guidelines and in compliance with applicable law(s) and regulations. This may include an inspection by the sponsor representative and/or regulatory authority representative at any time. The investigator must agree to the inspection of study related records by the regulatory authority or sponsor representatives and must allow direct access to source documentation.

Patient Information and Consent

Prior to the start of any study-specific screening procedures, examinations or treatments, the written informed consent form must be signed and personally dated by the participants as well as by the investigator leading the informed consent discussion. The investigator performing the informed consent discussion must be a healthcare professional trained in the protocol and its procedures. In obtaining and documenting informed consent, the investigator must comply with the applicable regulatory requirements and must adhere to ICH-GCP and to the ethical principles that have their origin in the Declaration of Helsinki (59th WMA General Assembly, Seoul, October 2008). The investigator must fully inform the patients of all pertinent aspects of the clinical study both verbally and in writing using the written information approved by the IEC/IRB. The patient information will be provided in a language comprehensible to the participants, and will not include any language that appears to waive any of the participants legal rights, or appears to release the Investigator, the Sponsor, or the institution from liability or negligence.

The patients will be informed about the nature, significance, risks and implications of the clinical trial as well as about their right to withdraw from the clinical trial at any time without giving any reason. The information will include a statement confirming that in the event a participants wish to withdraw their consent to the clinical study, no new information will be collected from the participants and added to existing data or to a database prepared for the clinical trial.

Participants will be given sufficient time after being given the patient information sheet to consider and discuss participation in the trial with friends and family. A contact number should be given to the participants should they wish to discuss any aspect of the clinical study. If a patient wishes to participate they should be asked to sign the consent form. The investigator will maintain a log of all participants who have signed an informed consent form. The participants medical records will also document that the informed consent form was signed and dated prior to any study-specific procedures being performed. The consent form includes acknowledgment that medical data derived from the study may be anonymously forwarded to the Sponsor, or the responsible authorities or federal authorities with compliance to relevant data protection provisions.

The right of the participants to refuse to participate in the trial without giving reasons must be respected. After the participants has entered the trial, the investigator must remain free to give alternative treatment to that specified in the protocol, at any stage, if he/she feels it to be in the best interest of the participants. However, the reason for doing so should be recorded and the participants will remain within the trial for the sole purpose of follow up. Similarly, the participants must remain free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing his/her further treatment.

DOCUMENT REVISION HISTORY

REVISION NUMBER	DOCUMENT CHANGE NUMBER	REASON FOR CHANGE	APPROVAL DATE MM/DD/YY	EFFECTIVE DATE MM/DD/YY

Recruitment strategy:

- Dr Sakel (PI) clinics and In-patient ward.
- Flyer (See 'RAPPER III- MS 010 Trial Flyer REV 0 FINAL') to invite patients to participate in trial to GPs, Consultants, MS Specialist Nurses
- Kent MS Therapy Centre
- Flyer in MS News Magazine, possibly in TV.
- Regional Brain Injury Conference, Canterbury chaired by Dr Sakel. The anticipated study will be discussed.

Acknowledgements:

We are grateful to continued support from Kent MS Therapy Centre, a Charity for people with MS and their families.

References:

1. Williams, G. Functional Ambulation Classification. Encyclopedia of Clinical Neuropsychology p.1105-1106 (2011) Springer New York
2. Powell, L. E. and Myers, A. M. (1995). "The Activities-specific Balance Confidence (ABC) Scale." Journals of Gerontology. Series A, Biological Sciences and Medical Sciences 50A (1): M28-34.
3. (Adapted from Tinetti et al, 1990 & Hill et al, 1996)
   Hill, KD. Schwartz, JA, Kalogeropolous, AJ and Gibson, SJ (1996). Fear of falling revisited. Archs Phys Med Rehabil 77, 1025-1029
4. Tinetti M, Richman D, Powell L. Falls efficacy as a measure of fear of falling. Journal of Gerontology 1990; 45: P239-43.
5. Hobart, JC, Riazi, A, Lamping, DL, Fitzpatrick, R, Thompson, AJ (2003)
   Neurology 60(12525714): 31-36.
6. J Neurol Neurosurg Psychiatry. 2004 Feb;75(2):266-9. The multiple sclerosis impact scale (MSIS-29) is a reliable and sensitive measure. McGuigan C[1], Hutchinson M.
7. Clin Rehabil. 2013 Aug: 27(8):728-40. doi: 10.1177/0269215512474942. Epub 2013 Feb 20. Ashford S1, Turner-Stokes L, Siegert R, Slade M.
8. Berg, K. Wood-Dauphinee S, Williams, JI : The Balance Scale: Reliability assessment for elderly residents and patients with an acute stroke. Scand J Rehab Med. 27 (1): 27-36, 1995
9. Simpson JM, Worsfold, C, Hunter, I (1996) Clinical Rehabilitation 10:354. Abstract.
10. Hawker, G. A., Mian, S., Kendzerska, T., French, M. Measures of adult pain: Visual analog scale for pain (VAS pain), numeric rating scale for pain (NRS pain), McGill Pain Questionnaire (MPQ), Short Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS) and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP) (2011) Journal of Arthritis Care and Research. Vol. 63. Issue supplement S11. November 2011. P. S240-252
11. Gregson, J,M., Leathley, M., Moore, A.P., A.K. Sharma, T.L. Smith, C.L. Watkins. Reliability of the tone assessment scale and the modified ashworth scale as clinical tools for assessing poststroke spasticity (1999). Archives of Physical Medicine & Rehabilitation. Vol. 80. Issue 9. P. 1013-1016.
12. Adams, M.M, Martin Ginis, K. A. and Hicks, A.L. (2007). The spinal cord injury spasticity evaluation tool: Development and evaluation. Vol.88. Issue 9 (p.1185-1192)
13. Johns, M. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. Sleep 1991. 14: 540-5
14. Balestroni, G. and Bertolotti, G. [EuroQol-5D (EQ-5D) : an instrument for measuring quality of life] 2012 Monaldi Archives Chest Disease 78 (3):155-9

15. Rehabilitation in Multiple Sclerosis. Jürg Kesselring Serafin Beer ACNR • VOLUME 2 NUMBER 5 NOVEMBER/DECEMBER 2002

16. MULTIPLE SCLEROSIS National clinical guideline for diagnosis and management in primary and secondary care. © 2004 Royal College of Physicians of London , ISBN 1 86016 182 0
17. Office for Disability Issues and Department for Work and Pensions, "Disability Prevalence estimates 2011/12" UK Government, 2014.
18. Allen K, Blascovich J. The value of service dogs for people with severe ambulatory disabilities. A randomized controlled trial. Journal of American Medical Association 1996;275:1001–6.
19. Stephens J, DuShuttle D, Hatcher C et al. Use of awareness through movement improves balance and balance confidence in people with multiple sclerosis: a randomized controlled study. Neurology Report 2002;25:39–49.
20. Wiles CM, Newcombe RG, Fuller KJ et al. Controlled randomised crossover trial of the effects of physiotherapy on mobility in chronic multiple sclerosis. Journal of Neurology, Neurosurgery & Psychiatry 2001;70:174–9.
21. Weinshenker BG. Natural history of multiple sclerosis. Ann Neurol 1994; 36(Suppl.): S6-11.
22. Active robotic training improves locomotor function in a stroke survivor Chandramouli Krishnan1,2,3*†, Rajiv Ranganathan1†, Shailesh S Kantak1, Yasin Y Dhaher1,2 and William Z Rymer1,2 Krishnan et al. Journal of NeuroEngineering and Rehabilitation 2012, 9:57 http://www.jneuroengrehab.com/content/9/1/57
23. Towards more effective robotic gait training for stroke rehabilitation: a review Andrew Pennycott1,2*, Dario Wyss1,2, Heike Vallery1,2, Verena Klamroth Marganska1,2 and Robert Riener1,2 Pennycott et al. Journal of NeuroEngineering and Rehabilitation 2012, 9:65 http://www.jneuroengrehab.com/content/9/1/65
24. National institute for health and Clinical Excellence. Rehabilitation after critical illness: summary of NICE guidance. Practice Guidelines. London: NICE 2009;338:b822. URL: http://dx.doi.org/10.1136/bmj.b822
25. National institute for health and Clinical Excellence. Rehabilitation after critical illness: summary of NICE guidance. Practice Guidelines. London: NICE 2009;338:b822. URL: http://dx.doi.org/10.1136/bmj.b822
26. National Guidelines February 2008; Chronic Spinal Cord Injury: Management of Patients in acute hospital setting. London. Royal College of Physicians. URL: https://www.rcplondon.ac.uk/sites/default/files/concise-chronic-spinal-cord-injury-2008.pdf
27. Health and Safety Executive (HSE) October 2014: Handling Injuries in Great Britain, 2014

28. Podsiadlo, D; Richardson, S (1991). "The timed 'Up & Go': A test of basic functional mobility for frail elderly persons". Journal of the American Geriatrics Society. 39 (2): 142–8. PMID 1991946
29. Martins, A.C., Pinheiro, J., Farias, B and Jutai, J. Psychosocial Impact of Assistive Technologies for Mobility and their implications for Active Ageing. (2016) Journal of Technologies, 4, 28 (p.1-9)

Participant Information Sheet

Study title: Rex robot Assisted rehabilitation exercise to enhance balance, mobility and uPPER limb function in people with Multiple Sclerosis "RAPPER III – MS"

Rex Bionics are now enrolling for RAPPER III, a 10 patient trial at East Kent Hospitals University NHS Foundation Trust (EKHUFT).

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take 10-20 minutes but this time will be dependent on your understanding and the questions you may have. Please feel free to talk to others about the study if you wish.

The objective of this feasibility study is to evaluate the overall device safety when used in a Clinical Rehabilitation Centre under the supervision of a physician and/or qualified rehabilitation specialist. The trial can be completed by patients over 6 sessions, each a week apart. The study will consist of walking in REX Bionics powered exercise device and completing a variety of therapy exercises the assistance of REX trained therapists. You will be asked to complete some questionnaires and other tests before the first session, after the 3rd session and finally after your 6th session.

This document is broken into 2 parts

Part 1 – tells you the purpose of this study and what to expect if you take part.

Part 2 – gives you more detailed information about the conduct of the study.

Part 1

What is the purpose of this study?

i) assess the feasibility and safety of undertaking a neuro-rehabilitation exercise program using a Rex robotic device within a controlled clinical environment (ease of use for both user and therapist
ii) Investigate the potential to improve balance and walking using Rex for people with MS
iii) Investigate the potential health benefits of this Rex Rehabilitation program
iv) Ascertain whether there might be a measurable impact on upper limb functional abilities

Why have I been invited?

You have been asked to participate in this study because you have a diagnosis of multiple sclerosis that fits the inclusion criteria of this study. There will be a number of assessments prior to trialling the device to ensure you fit the criteria to safely use REX. This is for your own safety.

Do I have to take part?

It is up to you to decide to join the study. We will describe the study and go through the information sheet. If you agree to take part, we will then ask you sign a consent form. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive. We are planning to enrol 10 people for this study.

What will happen to me if I take part?

Study Schedule

you will be asked to come to the rehab clinic for 6 sessions. The timing of these sessions vary and more detail is given below. Each session will be a week apart. Please ensure you wear **supportive fitting laced shoes,** a pair of comfortable sporting trousers/track suit bottoms and a light T-Shirt or Similar. If you have issues with the support structures of your feet you should consider using orthotics to offer added support. Please raise any concerns you have with your therapist conducting the research so further information can be provided to you.

- Enrolment – You will be asked some screening questions prior being enrolled in the study. If you are enrolled, you will be asked to complete 13 outcome measures (tests/questionnaires) in session 1, 4 questionnaires 2 days after session 3 and finally all 13 outcome measures (tests/questionnaires) in session 6. **(approximately 90 minutes)**
- Session 1 – you will be asked to come into the clinic to complete a number of tasks. **(approximately 150 minutes)**
    - Task 1: baseline medical assessment and giving informed consent:
        - A medical examination will take place along with a discussion around your current medical conditions and previous medical conditions to determine if you are safe to use REX.
        - You will be given a patient information sheet and ask to give consent if you would like to be included in the study. **You can withdraw at any time and do not have to give consent if you do not choose to.**
    - Task 2: Assessment against inclusion criteria:
        - You will be assessed against a number of different inclusion and exclusion criteria to determine whether you are appropriate for the study
    - Task 3: completion of pre-treatment outcome measures and questionnaires:
        - You will be asked to complete a number of scales and questionnaires. These will be repeated at the end of the study (during sessions 6). If you have any questions about any of these you should ask the investigator and the investigator will provide you with enough time and space to discuss everything. The outcome measures are listed below.
            - Activities-specific Balance Confidence (ABC) Scale
            - Modified Falls Efficacy Scale (MFES)
            - Multiple Sclerosis Walking scale (MSWS-12)

- Multiple Sclerosis Impact scale (MSIS-29)
- ARMA (arm activity measure)
- Berg Balance Scale
- Video of sit to stand and stand to sit (recorded twice)
- Video of walking – timed up and go (3 metres)
- Pain scale questionnaire (Visual Analog Score VAS)
- Modified Ashworth Score
- Epworth Sleepiness Scale (ESS) questionnaire
- EQ-5D Health State Questionnaire

    - Task 4: Measurements, fitment and mobilizing
        - A number of measurements will be taken to ensure you can safely use and fit the device
        - Once these have been taken you will be asked to transfer into the device. This will be timed.
        - On completion of a safe transfer you will be asked to stand up in Rex and walk 3 m, turn around and come back again, then sit back down on the chair. This will be timed.
    - Task 5: Exercise prescription
        - The investigator will work with you to determine an appropriate amount of weights/resistance that should be used for your treatment programs in the subsequent session.
- Session 2: Completion of a prescribed exercise program. **(approximately 45 minutes)**
    - Task 1: You will be asked to complete a set number of exercises that should last approximately 45 minutes.
- Session 3: completion of a prescribed exercise program. **(approximately 45 minutes)**
    - Task 1: You will be asked to complete a set number of exercises as you did in session 2.
    - Task 2: You will be asked to complete 3 questionnaires 2 days (plus or minus one day for flexibility with your schedule) after your exercise program. These will be completed over the phone with the investigator conducting the study. You will be given an envelope with all the questionnaires in so you have a point of reference. These questionnaires will be:
        - Pain scale questionnaire (Visual Analog Score VAS)
        - Epworth Sleepiness Scale (ESS) questionnaire

      You will also be assessed for your level of spasticity using the Modified Ashworth Score
- Session 4: Completion of a prescribed exercise program. **(approximately 60 minutes)**
    - Task 1: you will be asked to complete a set number of exercises as you did in the previous sessions
- Session 5: completion of a prescribed exercise program. **(approximately 60 minutes)**
    - Task 1: you will be asked to complete a set number of exercises as you did in your previous sessions
    - Task 2: You will be asked to complete a timed transfer to see if it has got any quicker since your first session.
- Session 6: Completion of follow up outcome measures and questionnaires. **(approximately 90 minutes)**
    - Task 1: You will be asked to complete all the same scales and questionnaires you completed in session 1 to see if there has been any improvement.

If you are unable to make the appointed visits in the time frame above, you will need to notify your physician or rehabilitation therapist.

What are the alternative to REX?

Currently REX is the only hands free, stable mobility device that allows you to walk forwards, backwards, left and right and side step. There are other devices on the market, however these do require crutches to keep you upright so you are unable to use your arms for other activities.

What are the possible disadvantages and risk of taking part?

- Accidental injury due to falling
- Skin issues such as bruising and redness
- Complications with you blood pressure
- Risks of breaks or fractures through falling
- Hip subluxation/instability
- Risk of Autonomic Dysreflexia with spinal cord injuries of T6 and above
- Risk of unintended bowel movement due to movement in REX

What are the possible benefits of taking part?

You might not get benefits from the study, however a greater understanding of whether the REX System can be used to rehabilitate patients with a similar condition will be gained from your participation in this study. This information may contribute to the development of new treatments for persons with Multiple Sclerosis.

What happens when the research stops?

After this trial, if you wish to continue receiving treatment of this kind for your general care unfortunately you will be expected to pay at an appropriate centre.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this will be provided in part 2.

Will the taking part in the study be kept confidential?

Yes. The records obtained while you are in this study as well as related health records will be strictly confidential at all times under the provisions of the 1998 Data Protection Act, to enable analysis of the study results. With your permission, you're GP and other doctors who may be treating you will be notified that you are taking part in this study. Further details are included in part 2.

In case of an adverse event your GP will be contacted and informed.

If the information in part 1 has interested you and you are considering participation, please read the additional information in part 2 before making any decision.

Part 2:

What if relevant new information becomes available?

Sometimes we get new information about the treatments being studied. If this happens, your local research team will tell you and discuss whether you should continue in the study. You can withdraw from the study at any time.

What will happen if I don't want to carry on with the study?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop, this would not affect the standard of care you receive.

In addition, the researchers, Rex Bionics, or your hospital or clinic may stop you from taking part in this study at any time:

- if it is in your best clinical interest,
- if you do not follow the study procedures,
- If the study is stopped.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting Dr Mohamed Sakel, the Chief Investigator for this study at EKHUFT.

Will You Be Paid For Participating In This Research Study?

No. But you will be provided with a £50 gift voucher for M&S on completion of the trial as a token of appreciation. Free parking will also be provided when you attend.

What Happens if You Are Injured or become unwell during the Course of this Study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the end of this form. The Hospital or Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?

If you have side effects from the study treatment, you need to report them to the researcher and your regular physician, and you will be treated as needed. If you have injuries directly resulting from the application of the study device or procedures, whether at your health care provider or another institution, the Sponsor, Rex Bionics will pay for appropriate medical treatment beyond that covered by your health insurance or other third party or government programs, at no cost to you. Your study doctor can help you obtain this reimbursement. Sponsor will not be responsible for deductibles and co-pays.

Authorization to Use and Disclose Protected Health Information

Your privacy is important to us, and we want to protect it as much as possible. By signing the consent form, you authorize the Hospital or Clinic and the investigators to use and disclose any information created or collected in the course of your participation in this research protocol. This information might be in different places, including your original medical record, but we will only disclose information that is related to this research protocol for the purposes listed below. This information will be given out for the proper monitoring of the study, checking the accuracy of study data, analysing the study data, and other purposes necessary for the proper conduct and reporting of this study. If some of the information is reported in published medical journals or scientific discussions, it will be done in a way that does not directly identify you.
This information may be given to other researchers in this study, including those at other institutions, representatives of the company sponsoring the study, including representatives in your country or other countries, or private, state or federal government parties or regulatory authorities in your country and other countries responsible for overseeing this research. These may include the US Food and Drug Administration, the Office for Human Research Protections, or other offices in your country within the Department of Health

Information Disclosed to Study Sponsor

The study data sent by the study doctor to the sponsor does not include your name, address, ID number, or other information that directly identifies you. Instead, the study doctor assigns a code number to the study data and may use your initials. Some study data sent to the sponsor may contain information that could be used (perhaps in combination with other information) to identify you (e.g. date of birth). If you have questions about the specific health information that will be sent to the sponsor, you should ask the study doctor.

This authorization lasts until the end of the study.

The study does not end until all data has been collected, checked (or audited) and analysed. Sometimes this can be years after your study visits have ended. For example, this could happen if the results of the study are filed with a regulatory agency like the local regulatory authorities or US Food and Drug Administration.

You may stop this authorization at any time by writing to the following address:

Chief Investigator

Address

If you stop authorization, the hospital or Rehab centre may continue to use your information already collected as part of this study, but will not collect any new information.

If you do not sign this authorization, or later stop authorization, you may not be able to

participate in the study.

Additional Information About Your Privacy

What Other Things Might the Sponsor do with Study Data?

In addition to the uses listed above, companies that sponsor studies often use study data for other purposes that are not part of the study. For example, the company might use the study data for research purposes to support the scientific objectives of the study described in this consent document, to learn more about the effects (good and bad) of any device or treatment included in the study, to better understand the injury or medical condition(s) included in the study, or to improve the design of future studies. Also, the company might share the study data with other companies it does business with. The company might do these things during the study, or after the study has ended, and would not have to ask for your permission to do so. The sponsor might still use study data, even after you stop your authorization, or the authorization expires, as long as the study data was collected before your authorization stopped or expired. The ways in which the study data could be used in the future may not be known now, so we can't give you the details.

What Will Happen to Your Data after?

Your data will be used as described for this study. When the study is done, they may be used for the purpose of publication, your name or identity will NEVER be revealed.

Who Can Answer Your Questions?

You can call	**At …**	**If you have questions or concerns about …**
Chief/Principal Investigator	**Phone:**	**Questions about the study tests and procedures**
Ethics Committee Health Research Authority	**Phone:**	**Research-related injuries or emergencies** **Any research-related concerns or complaints** **Rights of a research subject** **Use of Protected Health Information** **Any research-related concerns or complaints**

REX Bionics 5th Floor, 7 Swallow Place
London
W1B 2AG

Centre Name: East Kent Hospitals University NHS Foundation Trust

Study Number: RAPPER III – MS

Patient Identification Number for this trial:

CONSENT FORM

REX ROBOT ASSISTED REHABILITATION EXERCISE TO ENHANCE BALANCE, MOBILITY AND UPPER LIMB FUNCTION IN PEOPLE WITH MULTIPLE SCLEROSIS "RAPPER III – MS

Name of Researcher:

_____

Please initial all boxes

1. I confirm that I have read and understand the Participant Information Sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from **REX bionics,** from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐ ☐

4. I agree to my GP being informed of my participation in the study.

5. I agree to take part in the above study. ☐

Name of Participant Date Signature

Name of Researcher taking consent Date Signature

Appendix S2

Structure of trial sessions and Treatment Intervention

Total number of trial appointment sessions: 6

Sessions 1 and 6: Baseline data measurements and assessment.

Sessions 2 to 5: 4 treatment intervention exercise sessions

Treatment Intervention:

Exercise 1: Trunk and leg muscle strengthening through functional task practice of sit to stand and stand to sit inside Rex Rehab exoskeleton.

1 set of 10 repetitions.

If participant was able to synchronise their mental concentration with the physical task then the participant was requested to consciously join in with device to make task active-assisted (rather than passive) in the following manner.

Ascent from sitting position to standing position using Rex: Participant actively pushes down into their feet to synchronise using their legs as the Rex brings the individual up into a standing position. Participants were verbally requested to try to push down into their feet as the device brought the person up to standing.

Descent from standing position to sitting position using Rex: Participant actively pulls in their lower abdominal muscles whilst the device controls the descent into sitting. Participants were verbally requested to pull in their lower abdominal muscles as the device lowered the person.

For Exercises 2, 3 and 5, participants were verbally requested to pull in lower abdominal muscles during these exercises.

Exercise 2: Trunk strengthening by lifting alternate arms (with/ without weight)

Exercise 3: Trunk strengthening by lifting both arms (with/without weight)

2 sets of 10 repetitions.

Exercise 4: Trunk muscle strengthening with rotation to the left and then to the right

2 sets of 10 repetitions.

Exercise 5: Trunk muscle strengthening and balance practice by individual throwing and catching either a balloon or football for 2 minutes to trial therapist.

2 sets.

Exercise 6: Assisted walking practice inside the device for 3 metres in forwards direction and then backwards direction for a time period of 10 minutes.

Participant was requested to look forwards and maintain an upright posture. Then the participant was requested to initially feel and learn to adjust to the movement of how the Rex device brings the person forwards, when in walking forwards mode, accompanied with the trial neuro-physiotherapist keeping hands on the Rex device in order to stabilise it during movement. This practice was repeated in the same manner, while the device moved the person backwards, when in walking backwards mode. As the individual adjusted to the device movement and became familiar with the movement, then the participant was encouraged to actively draw in their abdominal muscles in addition to maintaining their vision forwards and maintaining an upright posture throughout.

From Session 2 to 5, all participants had the potential to be supported to increase the number of exercise sets depending on their progress as judged by the trial neuro-physiotherapist.

Appendix S3. Feedback comments from individual participants and care-givers

Participant Comments	**Care-giver Comments**
No confounding event during trial	Nice to see him smile, he was like a boy with a new toy in the Rex
Hoping for easier standing and any improvements	His confidence has gone through the roof
Huge improvements from day one of trial	He feels amazing, he's just happier, not grumpy anymore, makes life better for me
Easier movement in ankles in particular	I love the look on his face when he's in the Rex
An exciting experience	He kneels down for gardening because he now knows that he can get back up
Confidence has gone up 100%	He's started driving again, he hadn't driven in over a year
The independence was great, nice to stand up and have your hands free	It would be a real shame, if he couldn't use Rex again, it definitely made certain things in his body work better
Improved balance means the world, gives me more confidence and I can do things easier	Can move easier now, he can lift his feet up easier, so he is walking better
Bending over without the sticks is phenomenal,	Noticeable change in body and posture from the very first session
Now able to pick up a shoe from the floor, previously could not do this	Now keeps himself upright even when not in the Rex
I can stand up all on my own now	He got better and better each week
I have started going to the gym	There was nothing negative about being on the trial, we were impressed with the whole thing
Trying and doing more on my own without relying on others, I'm not scared to try now	
The trial has slowly improved everything	
Happier and more confident in doing things and trying anything	
Positive changes exceeded any expectation, wasn't expecting it to be quite so effective	
Parts of my feet work again now, that weren't before; I must keep this up to keep them working.	
I'd like to have one at home, a simpler version, I'd buy one.	
All the time that you are in the Rex it's working you, using a lot of your muscles, like a personal trainer	
Walking without the sticks is just amazing, can't carry anything when you have your sticks	
Back pain has reduced as a result of better posture, stronger core and body alignment	

Walked on the treadmill for a minute without aid Better bladder control More optimistic Improvement in quality of life Rex works different muscles, being upright with support, gives you confidence Instant improvements, absolutely amazing, beyond any expectations Everyone has noticed my improvements, big changes	
No confounding event I was hoping it would help with my balance and it really has My sister has also noticed a big difference in my balance The Rex was really scary when I first sat in it; I was also scared of not having control, the unknown scared me and being strapped in scared me. I didn't like the feeling of being strapped up and tied up, but felt safe with the straps I was completely fine as the trial went on, I wasn't scared I was up for using the Rex and being on the trial The machine walking for me felt weird By the second session I definitely felt safe and stable I noticed how upright I really was, I felt the machine had snapped my back into position Post-trial I'm sitting bolt upright Someone else was operating the controls as I couldn't see them, so no sense of independence Post-trial I'm walking with a frame at home, before I was in my wheelchair pretty much all the time I can get up and move about more I used my walker to the car, before I couldn't do that My balance feels pretty good Rex helps with the core muscles, I knew they were weak before	Rex has given her a confidence boost, she uses it to stay out of the wheelchair Sitting in a wheelchair does nothing for your core, but Rex really helps with core and posture Noticed improvements in posture, stability and balance Has helped keep her energy levels up Rex provides moderate exercise, would help with the muscle wastage that results from being in a wheelchair *With regular physio the fear of falling holds her back, in the Rex there is no fear of falling. We would try anything to help offset the effects of relapse or anything

Post-trial, I have the confidence to bend down and pick something up from the floor My improved confidence reduces the doubt No difference in sleep noticed Energized immediately after using the Rex, but felt tired afterwards. QoL has increased due to more confidence and consequently trying more things, makes me happy Have the confidence to get on the floor and play with the kids, knowing I can get back up I'd happily use it again; I don't want to end up all slouched again. No change in upper limb function No changes in sleep, pain, fatigue and bladder control No changes in cognition and memory A mood lifter, upbeat after session; not as withdrawn post-trial	
No confounding event during trial Hoping to see some progress, excited to take part, curious, not apprehensive; thoroughly enjoyed it, sad it's finished. Could stand up taller and straighter; nice to be upright, usually bent over on walker Would be able to make a cup of tea, do normal things, independence would come back Got more from Rex than normal exercises Biggest positive, was to stand up and move side to side confidently (Berg balance improved from14-17). I'm being honest I didn't see the effect. I wasn't aware of, nor did I feel the effects of the lesser self-reported confidence No change in self-reported confidence levels balance feels good During trial everything "sharpened up", but has reverted back since Improvements in speech that was noticeable by others No noticeable change in walking despite the improvements on the walking scale	Concerned about transferring in and out of the Rex and going to the toilet. Rex built up strength in legs and core, need good core for bladder. No noticeable improvement in balance Rex provides excellent support thus able to exercise stronger and harder; worked without worrying about falling. Was energized and it lasted for a few days after each session Being upright made her smile more Improvements were short lived Positive effects are fading post trial, but still mentally positive from trial. If continued then improvements would have been maintained. Small yet significant positive results.

Biggest negative of MS are the tremors Improvement on bladder control and tremors. Big reduction in fatigue and increase of energy Big improvements came from the ability to move legs more, changed into swimsuit quicker, bathed myself Stronger arms is the biggest outcome – sense of achievement from feeding myself, brushing teeth easier and holding cup/glass, even able to peel a Satsuma and take off the strings. More energy and enthusiasm as a result of slightly more enhanced ability No change in mood/happiness Quality of life improved from 80% to 100% on scale; I don't feel any difference in quality of life. If I had a Rex I'd do more, I'd walk further, have more confidence Independence; won't need someone by my side in case of balance I'd definitely use the Rex every day, it would have a place in my home Rex would replace my wheeled stroller I'd go for walks in the Rex; take the dog for a walk. Can't go to the loo in the Rex Energy went sky high and it cut down on fatigue to the degree that I can exercise twice a day. Getting more out of other exercises as a result of the trial Noticed improvements in the core after the first week of using Rex My physio's noticed improvements in standing up, walking tall and better arm movements. Shocked that on the third week I walked from car to house, un aided Rex brings you up to eye level, people talk to you; usually they ignore me and forget I'm there!	
No confounding event during trial	

Hoping for upper body and arm strength The whole process made me realize that I could do more than I thought; I tend to hold back to preserve energy The Rex really engaged my mind, into how each muscle and my whole body was moving. Felt solid and well supported in Rex Rex offered stability and balance which then allowed more movement during exercise. The concentration was good; it was an active process, whereas I had thought the Rex was going to do all the work. Felt privileged to be a part of the trial. Balance feels good Neurologist noticed improvements while assessing my toe to heel walk Increased awareness and improvement on balance One week post trial felt very very good, awareness of posture lead to more confidence. Confidence has waned a little one month post trial Walking and strength of walking is good, but usually pain in one foot. Didn't feel the foot pain while exercising in the Rex. Post-trial walking short distances without sticks Getting more done at home post-trial, doing more things (housework, gardening etc..), more active. An eagerness to try new things post-trial, resulting in trying gliding! An improvement in confidence as a result of good posture The increased confidence and the ability to do more was an unexpected outcome of the trial. Being more body aware and how I'm holding myself. Six weeks wasn't long enough, I'd continue to use it as part of my rehabilitation program; once a fortnight, a regular appointment would make me keep up the exercises in-between.	

Rex would allow you to stand at other people's height in social situations Felt less fatigued the days that Rex was used, in comparison to other exercise programs Memory has been better but not sure if it's because of Rex or the sunshine A big confidence booster; feeling more able Post-trial body strength and core strength has waned a little	
No confounding event during trial Better walking and better posture noticeable by family members and others I had improved during trial so I'm interested to use the Rex again as an exercise program I felt safe and stable throughout Walking and standing up with the robotic legs felt bizarre and surreal but enjoyable I did well with playing catch with the balloon; I enjoyed it and improved from 3 to 6 min. The trial helped a lot with my posture and core, as the exercises were more intense for the core I got very tired doing the exercises and using the Rex, I could feel that I'd done a workout Rex offers me an intense, safe form of exercise so less injury compared to regular exercise It was noisy, but I did enjoy controlling it myself I only feel a little change in balance, I've got a bit more balance; I still have to hold on to something if I want to lift my leg up. ABC scale (64 down to 58); perhaps I was feeling a little low on the day as my balance can be quite bad sometimes, good days and bad days. The most significant thing for me was the improvements in my posture A bit more strength in the muscles of the legs and arms. The positive is that I enjoyed it and I think it's helped me.	

I'd use the Rex for rehabilitation regularly it would help me with my posture, muscles and confidence. No changes in fatigue, sleep, pain, cognition and memory, bladder control or mood. Would there ever be a chance for me to use it again?	
No confound during trial Rex was a good supplement to regular physio I jumped at the chance to take part in Rapper III, no anxieties or worries My Physio says the trial has definitely helped for my posture Spasticity is negligible in my legs post-trial It gave me a feeling of standing up on my own, no help, a sense of independence It was nice to stand, my face lit up, being at normal height again Rex was easy to use, but hard to transfer in and out of Rex is rally dynamic, you have to do some of the work Not working on one limb in isolation, but using the core and legs while working on the arms; I can feel I've worked everything More mobility would improve certain aspects, it would allow me to do things I used to do; I'd go onto the golf course with the Rex The exercises were more important, walking was just a bonus I've had an improvement in standing post-trial; standing in a better position I'm now more aware of everything Post-trial I get up more easily; I see an improvement in movement. Post-trial, I have more flexibility in my left arm and I can reach further, that's a positive outcome Sit to stand is easier Not slouching as much Improvements in balance confidence, but on a bad day the confidence goes More control when going for sit to stand More confidence for getting in and out of the car	I noticed once he'd been up and down a few times, it reminded his muscles what to do Immediately post trial, he can pull and stand independently to get into the car, but a couple of hours later or the next day the improvements have gone Rex shows that the ability in the muscles are there, just need to work them Rex has a positive effect but it just doesn't last Most benefits were seen for getting in and out of the car The effects were short lived, they didn't last Post-trial, he's feet didn't swell up, he could get shoes on easily, big improvement Absolutely convinced that if he used the Rex for 2 or 3 months he would get to pull himself up on the grab bars like before We'd adapt our routine to use it regularly Sitting in a wheelchair 24/7 is not healthy I think Rex would improve his overall well-being If Rex was at the MS therapy center we'd go 2 to 3 times a week to use it, instead of once a week now.

The physiological impact of Rex is undeniable Post-trial no neurological pain, used to have shooting pains My Physio at the MS therapy center can notice an improvement I would use the Rex daily if I could I'd use the Rex instead of a wheelchair at home Posture has improved and improvements have been sustained post trial No change in cognition and memory More optimistic, more perky post-trial The trial was a good beneficial experience Rex would benefit all patients with MS Rex provides constant movement	
The spell of very hot weather during the trial was the only confound, as it affects the legs and makes the ankles swollen. Trial wasn't long enough to get lots of benefits I didn't gain an awful lot, my balance is as poor as it was pre-trial Rex was different and quite fun Rex felt quite safe, it was fun; it's strange as you feel quite taken over by it so I didn't feel in control Rex allowed me to put weight on my left leg which I don't usually do It's positive that it allows you to do things that you can't normally do It's a bit noisy but you get used to it, by the second session I was really comfortable The exercises in the Rex demand a lot of concentration; it's not a passive process you have to work quite hard. It's easy with MS to think you can't do a lot of things, but when you see that you can do it, and each time more, it gives you more confidence and that's a positive outcome. You realize that the rest of you still works; I realized that I can use my upper body more In the Rex, you have the freedom of using both arms.	

I felt safe, stable and confident in the Rex I was able to do all the exercises while in the Rex, and I achieved more each session. Testing your body, an achievement, an improvement It showed that my knee was giving way, but we were able to overcome that. My balance hasn't improved I'm going to get onto a program and get into the gym I realized I need to improve my balance by strengthening my muscles, which got stronger during the trial ABC scale (balance confidence) from 58 down to 43, but don't know why. I can't recover from a trip and when you fall you just hit the ground; fell badly a year ago. I can't walk well, and the wheel chair is dispiriting, it highlights your disability The fear of falling is greater than the actual chance of another fall. No changes felt despite the decrease in fall scale No pain, no fatigue and lots of energy; no changes Haven't actually noticed any difference physically, but enjoyed doing the trial I improved on the exercises, but wouldn't have noticed without all the counting and timing Doing more, must have come from a stronger core regardless of whether I noticed it or not myself. Contributing to help other MS sufferers Had no effect on posture Felt tired after sessions but not fatigued. The small positive effects motivated me to get more exercise done.	
Had a fall mid trial, but not too serious Hoping for knowledge and improvement in general and in strength in particular Post-trial able to bend down and pick up something from the floor Have noticed other little improvements post-trial, such as coordination It's been an interesting experience	He's had a mental boost from being on the trial, it has been good for his well-being. MS can overpower him mentally, so the trial was a good distraction Trial was constructive and positive; he has pushed himself to get here. The trial was a reason to get out of bed, to get up and go There is a very subtle change physically

Strange to be in the Rex; walking in it was different to my normal gate I felt safe; I knew I couldn't fall out I felt pretty confident I can only feel a very subtle change in balance post-tiral No changes in my walking ability My fall didn't negatively impact on balance Post-trial more control for sitting down instead of just falling into a chair Much more conscious of controlling my movements and able to do so. No change in sleep and pain Improvements in quality of life have come from taking part in a recent poker tournament not the trial. Playing cards has a better cognitive effect than reading a book for me. I'm always eager to try new things It's too early to say at this stage if I've benefitted from the trial. I'm doing some of the exercises and movement from the trial at home Taking up new physio as a result of taking part in the trial; it inspired me to do something productive I would use it for rehabilitation purposes once a month regularly No effect on mobility, stability or balance Given me more awareness, more conscious of doing things properly No effect on posture, just more conscious of staying upright Journey to the trial gave me fatigue My speech is worse with fatigue, so it got bad during the trial Awareness and knowledge is what I've got out of the trial	
One confounding factor: I experienced a serious fall before the last session of the trial which came just after hearing about a death in the family. I fell down because I was trying to do too many things at once. I informed the research team and they reported it as a Serious Adverse Event.	

Fall caused broken hip and damage to the cruciate ligament in my knee, which required immediate surgery and I was admitted into hospital for an immediate hip operation. Took part in the trial hoping for improvement in walking, as my right leg drags and it's heaver In Rex I could pick up my legs and walk, heavy leg felt fine Standing up right was the best thing, looking ahead, not worrying about my feet and the floor for balance Rex was quite noisy The 7 point decline on balance scale was due to my hip operation I have MS in my right leg and a new hip in my left leg Now using 2 crutches so feel more confidence for balance, feel safer ABC scale 20% increase, but increased confidence is due to two crutches as I can look ahead with them and not down to the floor Can't pick up something from the floor, the fear is there Can stand longer and do more, more confidence to complete a task Being in Rex, being upright, gives you more confidence, you realize that looking down is the problem Rex gave me a different perspective Had I not fallen, I think I had big improvements from using Rex Trial too short to have had a real big impact Now doing neuro-physio post trial, better than normal physio QoL down 20%, due to the operation, have lost my independence as I'm not driving; no social life now I'm stuck at home. Nice walking un-aided, very useful to have your hands free Rex would make my leg stronger over time, would use it regularly for rehab Would use the Rex at home, not sure about outside Felt energized after each session	

Had deeper sleep on trial days Mood lifting While on trial I wanted to get better, I wanted to improve my scores each week made me try new things.	
Botox injections for bladder control was the only confounding event during trial Hoping for more energy and improvement for walking Rex provided solid exercise, which was positive as I'm in a wheelchair most of the time Getting extra exercise, but no benefits afterwards Quite excited to be using something so innovative and I really enjoyed it. Felt safe, stable and confident in the Rex Controls were on the right hand side, so that made me anxious as I can't use my right arm Rex divides the body weight equally, therefore I felt I was being pulled around because of my weak right side It was unusual to use both sides properly and evenly Rex really made me work around my waist, which was a positive thing. Standing upright and really straight was the most positive thing about being in the Rex as I'm usually leaning over a bit. Very excited to be standing up (In Rex), suddenly on the same level as everybody else. Too many questions on the trial that wouldn't allow me to say what I wanted to say No change nor improvements in balance No changes in confidence in general or in regards to falling No changes in walking ability post-trial No change in quality of life I like to try new things and I'm always a positive person in general so no change there No change in overall well-being	Questions were all hugely subjective, therefore measurements were quite meaningless The one benefit of Rex, which no other instrument has given, was the upper body strength and core improvement. The Rex was solid, no other physio uses the upper body like that; it would build up the strength in the core and shoulders. You're straight, you're upright, utilizes the upper body like no other exercise. You have a boost of energy and a boost of enthusiasm; it works like a Placebo effect. Couldn't use it at home because of transfer issues, unless it was greatly improved and modified A huge positive psychological difference for being at eye level We would use it weekly as it strengthens and it would help physically. Post-trial there is no improvement in mobility No psychological or physical changes Benefits of Rex would depend on the person's MS at the starting point Our views are not hugely positive but glad we participated in the trial and were happy to contribute to research

I enjoyed the trial, it was a positive experience and definitely worth doing Standing up and being supported had an especially good effect on core muscles, it strengthened the core. Gave a general mood boost You get a chance to feel how it should be to stand up properly I think I would use it as a treatment program if it were available My confidence stems from the support I get from my husband	