CONFIDENTIAL

AVERT DOSE Intervention Protocol

A Phase 3, Multi-Arm Multi-Stage Covariate-Adjusted Response-Adaptive Randomised Trial to Determine Optimal Early Mobility Training after Stroke (AVERT DOSE)

Protocol No: 001-2
Version: 4.0
Date: 1 July 2024

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Definition of Terms

Stroke Onset: The date and time the patient first develops stroke symptom/s (*actual*) or if the time of stroke symptom onset is not known, then the stroke time estimate is the date and time the patient was last known to have no stroke symptoms (*estimated*).

Time to First Mobility Training (TTFM): The time to first mobility training is calculated from date and time of stroke onset (actual or estimated) to the date and time the patient first commences mobility training (MT). The first MT will occur within 48 hours and as soon as practical after recruitment.

Mobility Training (MT): Mobility training is where the patient is assisted and encouraged to actively participate in functional training tasks, including moving from lying to sitting, sitting over the edge of the bed, unsupported (active) sitting activities, sit to stand to sitting, transfers, standing and walking (indoors, obstacles, steps, stairs and outdoor surfaces) that support their relearning of balance or walking. MT is performed by the study **physiotherapists according to randomisation group and the daily level of functional ability**. The physiotherapist (PT) will progress training by selection of activities and increasing the intensity. MT activities are performed by study **nurses according to the days post stroke and daily level of functional ability**. Stroke unit staff such as health care assistants, occupational therapists, students and family/carers may assist with mobility training as directed by the study physiotherapists. There should be a bed rest period of at least 10 minutes after a physiotherapy MT session.

Assessment of Mobility**:** Assessment of functional mobility (sitting up, sit to stand, transfers, standing, walking) is usually performed before mobility training begins and informs the training protocols selected.

Other Assessments**:** Details of assessments performed in bed, sitting or walking (in bed or out of bed) by PT and nursing staff are not collected in this study. These include interviews (e.g. home environment), cognitive tests; and assessments of sensation, passive range of motion, mobility and upper limb.

Bed Rest*:* Time (minutes) when the patient is in bed lying down, or sitting supported in bed.

Frequency of Sessions: The number of mobility training sessions provided each day.

Intensity of Mobility Training: Intensity of PT mobility training is measured using the Borg Perceived Exertion Scale. The patient reports a score of 6 to 20 on the Borg Perceived Exertion Scale (Appendix A) at the end of a physiotherapist mobility training session. Patients unable to self-report are recorded as unable. Physiotherapists record a score of 6 to 20 on the Borg Perceived Exertion score for each type of training activity.

Physiotherapy and Nurse Record of Sessions*:* The minutes, intensity (physiotherapy only) and type of activities performed in each mobility training session will be recorded on the Mobility Training eCRF via REDCap. Paper Mobility forms will be used to temporarily collect the information until such time it can be entered online.

Type of Mobility Training Activities: Types of MT activities include sitting up/lying down, active (unsupported) sitting, sit to stand to sit (standing up, sitting down), transfers, early walking, walking and advanced walking. Examples are provided in Sections 5.3 and 6.2.

1 AVERT DOSE Intervention Protocol

This intervention protocol tells you how acute stroke patients who are eligible and have consented to the AVERT DOSE study need to be treated for physiotherapy and nursing mobility training (MT) during acute inpatient care,, in order to comply with the goals of the study.

In this study, recruited patients are randomly allocated, according to stroke severity (mild or moderate) to receive one of four MT intervention protocols. The four intervention groups will be delivered by study physiotherapists. Study nurses will deliver a protocol range of mobility training according to the patient's daily level of functional ability and days post stroke.

The mobility interventions outlined in this protocol are provided **instead of usual physiotherapy and nursing care mobility training**.

Physiotherapy MT is provided according to ***patient level of functional ability as assessed on a daily basis***. The dose each participant receives will differ according to the randomisation outcome and vary by the amount of minutes per sessions, and the number of sessions per day. The intensity of mobility training provided will be recorded.

Nurse MT is provided according to ***patient level of functional ability as assessed on a daily basis***. The ***Dose*** (number of sessions per day) will be varied according to the patient level of functional ability as determined by the MSAS. The minutes of mobility training provided will be recorded.

This protocol will be used by the nurses and physiotherapists to provide mobility training. This protocol conforms to the Template for Intervention Description and Replication (TIDieR) checklist.[1]

This document should be stored securely and accessed only by AVERT DOSE nursing and physiotherapy staff to prevent dissemination to other settings prior to trial results. The AVERT DOSE Trial Protocol No 001-1, details all other aspects of the study.

1.1 Purpose of the Intervention Protocol

The purpose of the intervention protocol is to:

- Provide study nurses and physiotherapists with guidelines to direct their management of all study patients
- Describe the underlying principles of physiotherapy and nursing mobility training, and outline the standards that must be provided to AVERT DOSE patients
- Detail the mobility training according to randomisation group
- Provide examples of AVERT DOSE mobility training that can be adapted to suit individual patients, and detail equipment that may be used
- Detail the mobility training physiological observations collected prior to, during and after mobility training for the first three days post recruitment
- Detail the recording standards for all AVERT DOSE patients
- Describe the importance of maintaining the study blinding, so that assessors for 3 and 6 month follow-up are unaware of patient group allocation
- Describe the evaluation of intervention fidelity

1.2 How to use the Intervention Protocol

This protocol is not intended to replace the clinical decision-making processes of the individual nurses and physiotherapists involved in treating the patients in this study but, wherever possible, they should be used to guide clinical decision-making. Key elements of dose, including minutes of therapy and frequency of sessions, should be closely adhered to.

2 Principles of Physiotherapy and Nursing Mobility Training

- Physiotherapy and nursing mobility training commences as soon as possible after recruitment and **within 48 hours** of stroke onset (Very Early Mobility Training).

- Physiotherapy (PT) and nursing mobility training outlined in this protocol is provided **instead of usual mobility training**.

- All mobility training is **task specific training** of functional activities such as active sitting up/ lying down, active (unsupported) sitting, sit to stand to sit (standing up, sitting down), transfers, standing (including standing balance), early walking, walking and advanced walking.

- All mobility training requires the patient to be **actively participating** in mobility training activities, actively using trunk and/or leg muscles and in an **upright position**.

- During the first mobility training session each day, the patient's **level of functional ability will be assessed** (using the MSAS) by a physiotherapist or delegate. The level of functional ability **remains constant for that day** and all submitted therapy and nurse recording forms should have the same MSAS level recorded.

- The dose provided by the **PT** (minutes for each session, and the number of sessions per day) is determined by the randomisation group. Dose must be adhered to wherever possible. If the protocol cannot be achieved, the reason for why the session could not be performed will be recorded. For each **PT session**, intensity and minutes of mobility training will be recorded for each activity (lying to sitting, unsupported sitting, sit to stand to sit, transfers, standing, early walking, walking, advanced walking). After each PT session, the patient will **rest on the bed for at least ten minutes**.

- The **number of nursing sessions each day** is determined by how many days the patient is post stroke (days 0 - 3 or days 4 onwards), and the daily assessment of functional mobility (using the MSAS). These must be adhered to wherever possible. If the protocol cannot be achieved, the reason for why the session could not be performed will be recorded. A nurse mobility session **must last more than 2 minutes** and be separated by 10 minutes to count as a new episode. For each **nursing session**, minutes of training will be recorded for each activity (lying to sitting, active (unsupported) sitting, sit to stand to sit (standing up, sitting down), transfers, standing, early walking, walking and advanced walking).

- The daily schedule should be provided from the time of randomisation, **for 14 days or until acute care discharge,** whichever is earlier.

- **Mobility training physiological observations** are completed prior to, during and after the first training session for the **first three days of physiotherapy** after recruitment and are detailed in Section 7.

- Other physiotherapy training such as moving in bed, upper limb training, joint passive range of motion, are performed according to usual care and are not the focus of this trial.

- If on the **first 3 days** after stroke onset the patient requires moderate or maximum assistance of others (functional mobility levels 1, 2 and 3) to move themselves from chair to bed, they should not be left to sit out of bed for longer than **50 minutes** each time.

- **Fatigue** should be monitored according to clinical practice. If the patient requires a rest from one activity, change to another activity with a different or lesser muscle demand. For example: if patient has fatigue in standing up and sitting down training, then change to lower energy tasks with reaching training in sitting. Short rests in lying (bed, plinth) or supported sitting (recliner, chair with back and/or arm supports) may be provided.

- During MT, the hemiplegic shoulder must be cared for according to Regional Stroke Guidelines.

- The Bedside Recording Form (Appendix C) can be used for each participant to provide a method of communication between physiotherapy and nursing staff.

3 First Mobility Training Session

Following enrolment to the trial (0-48 hours post stroke onset), the patient should commence the first mobility training, including the physiological assessment (Section 11). This session is a physiotherapist session performed in conjunction with study nurses wherever possible. All patients should complete the first mobility training session within 48 hours of stroke onset. If the first mobility training session cannot be completed within 48 hours, the reason/s why will need to be documented as a Protocol Deviation.

4 Level of Functional Mobility

The patient's level of functional mobility using the Mobility Scale for Acute Stroke (MSAS) will be assessed prior to the first mobility training session by the study physiotherapist or nurse. During the first mobility training (MT) session for each day post stroke, the physiotherapist or nurse will re-assess the patient's level of functional mobility and set the patient's level of functional mobility for that day.

Based on the findings of the MSAS, the patient's functional ability should broadly fit into one of the four levels of functional ability, as summarised below:

Level	**Patient Functional Mobility Description**
1 – This is equivalent to **sitting from supine MSAS** Score of 1-3	**Fully dependent.** Unable to sit on the edge of the bed without assistance of 1 – 2 people, to moderate assistance one person. Patient scores MSAS gait =1, unable to walk or no contribution.
2 – This is equivalent to **sitting from supine MSAS**	**Moderate-high dependence.** Can sit on the edge of the bed but requires minimal assistance, supervision or is independent. Able to stand with assistance. Patient scores MSAS gait =1, unable to walk or no contribution.

Score of 4-6	
3 – This is equivalent to **gait MSAS** Score of 2-3	**Moderate dependence.** Able to walk with moderate-maximum (1-2 people) assistance.
4 – This is equivalent to **gait MSAS** Score of 4-6	**Low/no dependence** Able to walk with minimal assistance, supervision or independent.

5 Physiotherapy Mobility Training and Examples

Physiotherapy (PT) mobility training sessions are provided **instead of usual physiotherapy mobility training**. PT training occurs Monday to Friday. Saturday and Sunday training can occur in sites where routine PT staff are available and will be recorded. A MT session is defined as minutes of continuous active mobility training which is determined by the randomisation, followed by a period of bed rest of at least 10 minutes. During the session, the physiotherapist will progress training by selection of activities and intensity. If the PT assesses the patient as fatigued during training, short rests within a mobility session can be provided as needed, but each rest period **should be no longer than 2 minutes**. Rests during training may be provided in lying down, or supported sitting. (e.g. fully supported chair). Time in resting should not be counted towards the total MT time. For example, a 10 minute MT session could be 6 minutes sit to stand and standing training, 1 minute rest in supported sitting, then 4 minutes of training active (unsupported) sitting.

5.1 Mobility Training Dose

5.1.1 Mild Stroke Severity (Baseline NIHSS 0-7)

Mild patients will be randomised to one of four PT treatment groups (Group A, B, C or D).

Group A 10 minutes/once per day (**10by1**)
Group B 10 minutes/twice per day (**10by2**)
Group C 20 minutes/once per day (**20by1**)
Group D 10 minutes/four times per day (**10by4**)

5.1.2 Moderate Stroke Severity (Baseline NIHSS 8-16)

Moderate patients will be randomised to one of four PT treatment groups (Group E, F, G or H).

Group E 10 minutes/once per day (**10by1**)
Group F 10 minutes/twice per day (**10by2**)
Group G 20 minutes/once per day (**20by1**)
Group H 10 minutes/three times per day (**10by3**)

5.2 Mobility Training Intensity

Physiotherapists will set the intensity of each training activity using the Borg[2] Rating of Perceived Exertion (RPE) using the number range 6-20. (Low: 6-10, Moderate: 10-14, Vigorous: > 14) The

patient will be asked to rate their perceived exertion at the conclusion of each session, using the Borg[2] rating scale, and this will be recorded.

During the first 3 days post stroke, mobility training may be delivered at a low intensity. **The PT should increase the intensity of mobility training within the session/s as clinically able with the patient.** After 3 days post stroke, the PT can increase the intensity of training as able to create an achievable but reasonably challenging work rate for the patient.

5.2.1 Physiotherapist Rating of Patient Received Exertion

During mobility training sessions, the PT monitors the intensity of each activity. Things the PT may monitor include respiratory rate, heart rate, breathing effort, ability to talk, sweating, if patient is feeling hot, if face is flushed, if patient wants to rest. At the end of the session, the PT will rate the intensity as low, moderate or vigorous for each activity on the Mobility Training eCRF. For example, if the majority of time for early walking training the patient was working at moderate intensity, record as moderate intensity.

	Low Intensity RPE $_{6\text{-}20}$ of 6-10; Activities that take little effort e.g. active sitting, sitting balance, low effort walking	***Moderate Intensity*** $RPE_{6\text{-}20}$ of 10-14; Requires a moderate amount of effort and noticeably accelerates the HR	***Vigorous Intensity*** $RPE_{6\text{-}20}$ of >14; Requires a large amount of effort, causes rapid breathing and a substantial increase in HR
Observations during mobility training	No/minimal change in respiratory rate No/minimal change in heart rate Speak comfortably whilst training Managed easily Not effortful Performed well No fatigue Rest not required	Increased respiratory rate Increased heart rate Able to maintain conversation May require rest break to continue	Shortness of breath, increased respiratory rate Increased heart rate Difficulty talking whilst training Working through rest Close to maximum effort Muscular fatigue Sweaty, face flushed, feeling hot May be nauseous due to exercise

Notes.

- For someone with cardio-pulmonary disease, use the same indicators for low, moderate and vigorous exertion. For example, a patient may be at moderate intensity doing sitting activities.
- If a patient reports pain during any session, the session should be stopped to assess the source of pain, including cardiac causes.

5.2.1 Patient Rating of Perceived Exertion

Using the Borg RPE Scale, at the end of each physiotherapy session, ask the patient "How physically hard did you work in the session?" See Appendix A.

5.3 Mobility Training Examples

Examples of mobility training are described below, including examples of how to change intensity.

5.3.1 Active lie to sit to lie Examples

Patient is in bed, actively encouraged to roll over to side lying then move to active sitting up, feet over the edge of the bed, reverse, and repeat.

- Changing bed head position, 60 degrees up, to flat, can increase exertion
- Changing number of pillows can have the same effect
- Lying on unaffected side, affected side, can alter effort
- Use of bed aids or not using aids can change effort
- Change speed (faster or slower may increase effort)
- Increase/decrease the number of repetitions
- Amount of assistance i.e. therapist (and nurse) assisting with impaired upper limb, legs, head and trunk, to patient assisting with all aspects, and therapist providing just enough assistance to achieve activity. Therapist can get patient to focus on one aspect, then add e.g. head and/or trunk and/or leg movement, and/or moving bedding and/or controlling impaired arm position, and/or speed and safety to achieve final position.

Note. Moving in bed activities alone (eg. rolling, bridging, bed exercises, moving up/down/across bed) are **not** included as mobility training sessions.

5.3.2 Active (Unsupported) Sitting Examples

For active sitting, the patient is seated without a back support. Active sitting may be on a bed, plinth, or sitting forward away from the back of a chair.

- Sitting upright over base of support/balanced sitting/postural alignment
- Increasing the time actively sitting
- Turning head, turning head and trunk within base
- Using arm/s, not using arm/s for support
- Feet on floor, feet off floor
- Legs wide to narrow
- Reduce base of support (smaller chair surface, increase height of bed)
- Moving trunk/head outside base of support (leaning forward to feet; leaning back; lateral to left and right), return to active sitting, postural alignment
- Reaching inside and outside base of support (to left, right, to feet, turning head/body behind). Increased object weight in upper limb
- Functional sitting balance activities (e.g hair combing, brush teeth, having a drink, dressing/undressing upper body, putting on a shoe). Increased object weight in upper limb.
- Turning towards unaffected side, to affected side
- Change speed. Faster or slower may increase effort

- Increase the number of repetitions
- Amount of assistance i.e. therapist assisting with impaired upper limb, legs, head and trunk, to patient assisting with all aspects and therapist providing just enough assistance to achieve activity
- Soft bed/chair/surface (e.g. foam under bottom, wedge)
- Tilting/moving/rocker surface (sitting on a ball, rocker)
- Patient sitting in deep chair, patient to move forward away (may require weight shift and buttock/leg forward movement) from trunk support

5.3.3 Sit to Stand to Sit (Standing up, Sitting down) Examples

- Change height of surface from floor
- Change sitting surface
- Change start position (sitting back in chair, edge of chair)
- Change feet position, unaffected leg forward to increase push down effort from affected leg
- Put a small step under unaffected leg to increase push down effort from affected leg
- Change speed. Faster or slower may increase effort
- Increase the number of repetitions
- Postural alignment/weight bearing
- Amount of assistance i.e. therapist assisting with legs (positioning of feet), head and trunk, to patient assisting with all aspects, and therapist providing just enough assistance to achieve activity.

5.3.4 Transfer Examples

Transfers are standing up, stepping forwards/sideways/backwards and sitting down. Transfers must include stepping (not a swivel transfer).

- Increase the number of repetitions
- Change height of surface from floor
- Change sitting surface
- Change start position (sitting back in chair, edge of chair)
- Change feet position, unaffected leg forward to increase push down effort from affected leg
- Change speed. Faster or slower may increase effort
- Amount of assistance i.e. therapist assisting with legs (positioning of feet), head and trunk, to patient assisting with all aspects and therapist providing just enough assistance to achieve activity.

5.3.5 Standing and Standing Balance Examples

Feet are stationary during training.

- Postural alignment/ balance standing
- Head and trunk turning
- Increase weight bearing on affected leg e.g. unaffected leg standing on soft surface (foam) or block, heel up on unaffected leg
- Balance board/plate activities
- Weight shift side to side
- Change feet position with weight shift (eg. step stance, wide stance)

- Reaching in standing, turning, different feet positions. Functional activities (e.g hair combing, brush teeth, having a drink, dressing/undressing upper body, put away clothing in draws)
- Push off practice without stepping
- Change speed. Faster or slower may increase effort
- Increase the number of repetitions
- Amount of assistance i.e. therapist/s assisting with legs (positioning of feet), head and trunk, to patient assisting with all aspects, and therapist providing just enough assistance to complete activity.

5.3.6 Early Walking Examples

Feet/legs are moving +/-head, trunk, feet and/or arms, but not propelling body continuously forward.

- Postural alignment/ weight bearing/ weight shifting
- Standing and stepping, forwards, sideways, backwards (such as during transfers)
- Push off practice with stepping
- Change speed. Faster or slower may increase effort
- Increase the number of repetitions
- Amount of assistance i.e. therapist assisting with legs (positioning of feet), head and trunk, to patient assisting with all aspects, and therapist providing just enough assistance to achieve activity.

5.3.7 Walking Examples

Walking on a flat indoor surface. Continuous movement of leg and body in a forward direction, including turning.

- Flat indoor surface gait training
- With/without gait aid (stick, frame, ankle foot orthosis etc.)
- Change speed. Faster or slower may increase effort
- Increase the distance, increase stride length
- Amount of assistance i.e. therapist assisting with legs (positioning of feet), head and trunk, to patient assisting with all aspects, and therapist providing just enough assistance to achieve activity.

5.3.8 Advanced Walking Examples

Continuous walking with body turning, walking backwards, steps, stairs, changing floor surfaces, stepping over or around objects.

Notes.

Equipment such as hoists, transfer belts, sit to stand devices, gait aids, balance equipment and supported treadmill walking may be used during mobility training, see Section 15.1.

- Preparation time for mobilisation training is not counted as part of the session (i.e. explaining to patient, setting up equipment)
- Equipment may place or support patient in position (passive equipment) ready to start training (e.g. hoist)
- If equipment is being used during training, patient should be actively assisting (e.g. moving affected leg during supported treadmill walking)

6 Nurse Mobility Training Activities and Examples

Standardised nurse MT activities are provided **instead of usual nursing mobility care**. The number of sessions each day is provided according to the number of days post stroke, (0-3 or 4 onwards) and the patient's assessed level of functional mobility for that day.
Nurse MT activities are provided and recorded Monday to Sunday. One nurse session comprises functional mobility activities that must be greater than two minutes' duration. A MT session is considered a new session if it is separated by at least 10 minutes from another.

6.1 Standardised Nursing Mobility Training Activities

Level of Functional Mobility	**Number of Sessions Day 0 - 3 post stroke**	**Number of Sessions ≥ Day 4 post stroke**
Level 1. Fully Dependent This is equivalent to sitting from supine, MSAS score of 1 - 3	0-2 sessions	1-3 sessions
Level 2. Mod-Max Dependence This is equivalent to sitting from supine, MSAS score of 4 - 6	1-2 sessions	2-5 sessions
Level 3. Moderate Dependence This is equivalent to gait MSAS score of 2 - 3	1-4 sessions	2-5 sessions
Level 4. Low/no Dependence This is equivalent to gait MSAS score of 4 - 6	2-4 sessions	4-6 sessions

6.2 Mobility Training Activities for Nurses

Examples of mobility training activities are described below. Equipment such as a transfer belt or standing transfer equipment may be used but patient must be actively using trunk and/or leg muscles.

6.2.1 Sitting up, Lying Down Examples

- Active moving from supine and/or side lying to sitting on the edge of bed, and return.

6.2.2 Active (Unsupported) Sitting Examples

- Sitting over edge of bed/sitting in chair with back unsupported to change top half of clothes, brush teeth/ brush hair/ wash face, use bottle

- Sitting over edge of bed/sitting in chair with back unsupported for drink, snack, breakfast, lunch, dinner, take meds.

6.2.3 Sit to Stand to Sit Examples

- Standing up and sitting down from the bed or chair
- Standing up from different chairs (low chair, deep seat, soft seat, no arms on chair).

6.2.4 Transfer Examples

- Standing up, stepping forwards/sideways/backwards and sitting.

6.2.5 Standing and Standing Balance Examples

- Standing up to dress lower body
- Standing at basin for grooming. Shaving, drying hair, combing hair, brushing teeth, applying makeup (can be wheeled to bathroom)
- Standing after using toilet/ commode e.g. to attend to own personal hygiene
- Standing to use bottle/ urinal
- If bedroom or other ward area has dynamic view of landscape, people etc., standing with assistance looking at view.

6.2.6 Early Walking Examples

- Walking a few steps.

6.2.7 Walking Examples

- Walking to bathroom, to lounge area, to lifts
- Walking around the ward with family

6.2.8 Advanced Walking Examples

- Walking and carrying things e.g. makes own drink or collects meal tray
- Walking and turning
- Walking up and down stairs
- Walking on outdoor surfaces, gravel, concrete, pavers etc.
- Walking to coffee shop/ cafe with family.

7 What if Planned Session/s Cannot be Provided to a Patient?

If a MT session cannot be delivered at the planned time due to competing therapy or ward procedures, try to deliver the session/s later in the day or organise another trained staff member to complete the session/s. Missed sessions on one day should not be added to the next day of training.

Other factors that affect a patient's ability to mobilise may include (but not be limited to): (i) an adverse event leading to a mobility training restriction for a period of time e.g. acute myocardial infarction, lower limb fracture, pneumonia, carotid endarterectomy; or (ii) a deterioration leading to palliation.

In the case of a temporary interruption to MT due to an event similar to those listed above, training ***should recommence as soon as possible***. Where training is interrupted for more than one day, the patient will be monitored every day to see if training can recommence. The patient is not discharged from the intervention schedule unless the patient drops out of the intervention, is documented as palliated or dies. Refer to Section 10 for reasons for dropout.

If a session is missed, is not delivered according to protocol or the patient has an interruption to the training schedule, reasons for why will be completed on the eCRF. Complete an Adverse Event (AE) or Important Medical Event (IME) eCRFs (as required).

8 End of Intervention

The patient receives the randomised daily MT schedule until the patient is discharged from acute care, or the patient has received 14 days of intervention (whichever is earlier).

9 Adverse Events (AEs) and Important Medical Events (IMEs)

Any Adverse Events (AEs, serious or not serious) or Important Medical Events (IMEs, serious or not serious) occurring during MT should be reported according to AVERT DOSE Protocol No 001-1 v1.0 31 October 2018.

10 Dropout of Intervention

The patient (or person responsible) may decide to drop out from the mobility training schedule. If this occurs, trial staff will request permission to continue to record mobility training provided by usual care hospital staff and ask if the patient would still be happy to be followed-up at 3 and 6 months. Please discuss any potential dropout with the site investigator and trial manager within 24 hours.

11 Physiotherapy Mobility Training Physiological Observations

Physiological observations are recorded in four body positions prior to, during and after the first physiotherapy MT session of the day for the first three days of PT mobility training after recruitment at approximately the same time of day where possible. For example, if the patient is recruited on a Thursday, observations are recorded on Thursday, Friday and Monday (no physiotherapy on the weekend).

The body positions are: (1) supine, (2) sitting, (3) standing (if able); and (4) supine.
Temperature is recorded prior to the session at body position 1, supine. For body positions 1-4, repeated measures of blood pressure (BP), heart rate (HR) and oxygen saturation (SO_2) are recorded. If the patient has mobilised out of bed prior to entry in the trial, these observations will still be performed for the first 3 days after recruitment.

Clinician judgement is still required when assessing a patient's suitability to get out of bed and commence mobility training. If the clinician decides the patient should not commence training, body position 1 (supine) is completed on the Mobility Training eCRF. If, in the clinician's judgment, **the patient is not tolerating the mobility training session the patient is returned to bed**.

Any incidences of being unwell is recorded as the reason for a missed/aborted session and as an Adverse Event. Examples include becoming less responsive, dizziness, vertigo, nausea, vomiting, headache, pale, clammy or other reasons. Use clinical judgment to decide when to commence mobility training again and according to the training group randomisation.

If the patient is unable to be mobilised, or returned to bed without completing all required observations, supine and any other mobility observations are recorded. Three days of observations prior to, during and after mobility training are required, whether complete or incomplete, and are to be reported on the eCRF. If the mobility observations are not able to be recorded for the first session of the day, they can be taken at subsequent sessions on that day if possible.

11.1 Physiological Observations

11.1.1 Supine in Bed (for at least two minutes)

Patient is supine in bed or with back of bed raised to less than 30 degrees (one to two pillows supporting head). After two minutes, record:

(i) Temperature
(ii) Systolic and diastolic blood pressure (BP is measured in the unaffected arm)
(iii) Heart rate
(iv) Oxygen saturation

Commence mobility training session.

11.1.2 Standing if Able (done as soon as standing)

If the patient is level 3 or 4, assist the patient to stand and repeat the observations as soon as standing. If the patient cannot stand (level 1 or 2), then these observations are not required. (See figure x) Return to training or stop according to the training group randomisation.

11.1.3 Sitting in a Chair (after ten minutes of mobility training)

After mobility training for 10 minutes, sit the patient in a chair and record:

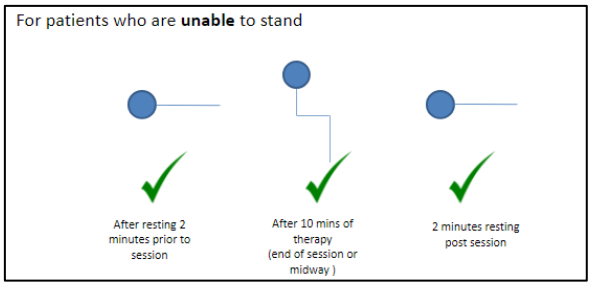
(i) Systolic and diastolic blood pressure (BP is measured in the unaffected arm)
(ii) Heart rate
(iii) Oxygen saturation

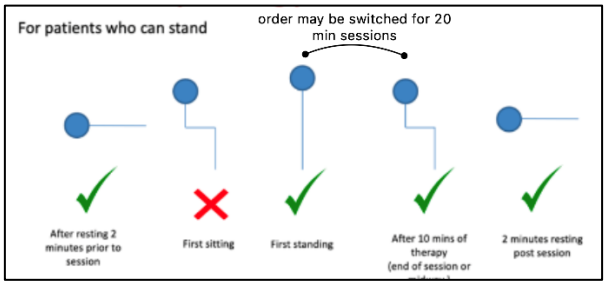
This will either be the end of the session or mid-session if patient allocated to 20 minute group. (see figure below)

11.1.4 Supine in Bed (at two minutes)

After training session is completed, the patient is supine in bed or with back of bed raised to less than 30 degrees (one to two pillows supporting head). This position should be the same for Observation 1 and 4. After two minutes supine, repeat observations

When measurements are to be performed:





If the participant is randomised to receive 10 minute sessions and the participant stands during the session, the standing measure will be done first and recorded on the therapy recording form accordingly.
If the participant is randomised to receive 20 minute sessions, it will be indicated on the therapy recording form which measure (standing or sitting) was performed first. (as 10 minute sitting measure may occur prior to standing).

12 Recording

12.1 Patient Medical Record

On the patient medical record, nursing and physiotherapy assessment of function, mobility and therapy details should be recorded. Records should document the date and time of reporting according to hospital procedures. **Do not provide information** on the minutes provided, or the number of sessions delivered as this may bias the blinded assessor.

12.2 Electronic Case Report Forms (eCRFs)

12.2.1 Mobility Training eCRF

Study nurses and physiotherapists will record each MT session using the **Therapy Recording Form** (Appendix B) and entered into REDCap. Staff will complete the paper forms and transcribe this information to Project 3 (Dose Treatment) in REDCap as soon as practical after MT. If a correction or data clarification to the eCRF is required, these are made using the eCRF.

Mobility activities (e.g. walking) that are self initiated by the patient or someone else during the intervention period and are observed by the trial staff will be recorded as an observed session on REDCap.

Any interruption to the training schedule should be documented on the relevant therapy or nurse recording form. One **Therapy Recording Form should be submitted for each missed per protocol session** with reason/s. For example, on a weekday public holiday where training according to the protocol is not possible, please submit one Therapy Recording Form for each missed session and

indicate reason. These will **not be recorded on the protocol deviation page** as it may unblind follow up assessors.

Three complete (or incomplete) MT Physiological Observations (Section 11) will be recorded on the Therapy Recording Form and transcribed to REDCap (Appendix B). Missed physiological observations will be recorded on the protocol deviation form.

If the patient does not receive their first intervention within 48 hours of onset of stroke, a protocol deviation will be completed.

12.2.2 End of Intervention eCRF

The End of Intervention eCRF is completed when the patient is discharged, or after 14 days of intervention (whichever is earlier). Reasons for end of intervention include: patient in stroke unit for 14 days or more, patient discharged home, patient transferred to inpatient rehabilitation, documented palliation, death, transfer to another ward, transfer to another hospital, other.

12.2.3 Dropout eCRF

The patient (or person responsible) may decide to drop out of the intervention but still remain in the trial for follow-up at 3 and 6 months. A patient (or person responsible) may also decide to withdraw from the trial with no further follow-up. Please discuss any dropout with the site investigator and trial manager within 24 hours. Following this discussion, the End of Study eCRF is submitted.

13 Blinding

Blinding (keeping people unaware of the group patients have been allocated to) is **vital** for any randomised controlled trial. We **must** keep patients and their families unaware of the intervention group. The following measures must be followed to maintain blinding for the AVERT DOSE study.

a) **Never tell** a patient or their families the group to which they have been randomly allocated, *even if they ask*.
b) **On the patient medical record, detail the date and time of one physiotherapy session per day or as per your standard care entry. Please document all relevant assessment and treatment details.** Do not provide information **on the minutes provided, or the number of sessions delivered.** Never tell anyone who doesn't need to know the patient's group, *even if they ask.*
c) AVERT DOSE staff need to ensure that other stroke unit staff are not provided details of trial interventions.
d) The blinded assessor assigned to this trial should be remote from the ward in which the trial will take place so as to not witness treatments that patients are receiving.
e) The **blinded assessor**, who may come to conduct assessments, **must never be told** the group to which patients are allocated. The assessor has been trained in what they can and cannot ask participants, therapists and other staff they encounter.
f) The blinded assessor will announce if they are visiting the ward for any reason, to minimise the chance of them witnessing any intervention sessions. Every effort should be made by AVERT DOSE staff to ensure that sessions are not witnessed by the blinded assessor.

14 Intervention Fidelity

Evaluation of intervention fidelity is an important aspect of the trial protocol.[3] We will report two components of intervention fidelity. Firstly, the component delivered by the researchers' education and training of staff, and secondly, the adherence by therapists and nurses to the planned intervention by group.

A record of all education and training provided to relevant physiotherapists and nurses will be maintained.

For all staff involved in mobility training with participants, a peer reviewed assessment of 2-3 training sessions delivered will be undertaken by the principal investigator or delegate. The staff member will complete the training session with the participant and complete the therapy recording form for the session. The principal investigator or delegate will observe the training session and complete a therapy recording form for the session. These will be submitted to the research team for review and feedback to the staff. Throughout the trial, peer assessment will be randomly undertaken with the goal of monitoring 5% of all therapy sessions.

All mobility sessions will be documented in detail on a therapy recording form, for the time, type and intensity of the session which is subsequently transcribed into REDCAP®. These data will be centrally reviewed for adherence to the protocol and feedback provided to site staff on a regular basis. The trial monitors will visit sites on a regular basis and where issues with fidelity are identified, additional training and peer reviewed sessions will be conducted.

15 Equipment

15.1 Local, Regional and National Policies

Local hospital, regional and /or national health and safety policies regarding the use of equipment to move the patient (e.g. beds, standing hoists, standing frames, tilt tables, chairs, lap trays, gait aids, arm supports, safety belts etc.) will be followed. Local infection control policies should be adhered to during assessment and mobility training procedures.

15.2 Timers

Timers will be used to time physiological assessments, session length and rest periods.

15.3 Physiological Equipment

Usual ward equipment will be used to measure temperature, blood pressure, heart rate and oxygen saturation.

15.4 Training Equipment

Equipment to support mobility training, such as supported walking devices, can be used. The principle of equipment use is that the patient must be actively training in functional activities.

16 Professional Conduct

The participant's health and well-being during participation in the trial should be monitored by research staff as a routine part of clinical practice. The guidelines in this protocol are not intended to replace clinical decision-making processes of nurses and clinicians involved in treating patients in this study, but, wherever possible, they should be adhered to. Nurses and clinicians should always make decisions on patient care based on their professional judgement. Where there are clinical practice issues which affect the conduct of trial, these must be raised with the trial manager.

Appendix A. Borg Rate of Perceived Exertion Scale

At the end of each session, the PT is to ask 'how physically hard did you work in the session?' The patient can point to the scale or verbally provide a score.

The patient provides a score from 6 to 20 according to the definitions below:

Ratings of Perceived Exertion

6
7 = Very, very light
8
9 = Very light
10
11 = Fairly light
12
13 = Somewhat hard
14
15 = Hard
16
17 = Very hard
18
19 = Very, very hard
20

From: Borg G. Perceived exertion as an indicator of somatic stress. *Scandinavian Journal of Rehabilitation Medicine* 1970; 2-3:93-98.

Note: If the patient is unable to report perceived exertion, score = unable

The PT can provide additional information, including gesture to ensure the patient understands the scale. For example: This is not about how hard you are concentrating, because I know you have been working as hard as you are able. This is about how much muscle effort, heart pumping and breathing effort you are doing.

Appendix B. Mobility Training Recording Forms

AVERT DOSE Therapy Recording Form

Site #: ☐☐ **Patient #:** ☐☐☐ **Patient Initials:** ☐☐☐

Date of session: / / **Session number:** ☐

Start of session time: : (24 hour format)

Therapist Initials: ☐☐☐ **Patient's functional level:** ☐

At start of session, participant found in: ☐ Bed ☐ Chair

Provided by: ☐ No assist/Obs ☐ Nurse x1 ☐ Nurse x 2 ☐ PT x 1 ☐ PT x 2
☐ Other Allied Health ☐ Health Care Assistant x 1 ☐ Student ☐ Family/Other

ENTER TIME IN MINS AT RELEVANT INTENSITY			
ACTIVITY/INTENSITY	Low	Moderate	Vigorous
Hoist			
Lie to sit to lie			
Active sitting			
Sit to stand to sit			
Transfers			
Standing			
Early walking			
Walking			
Advanced walking			

PHYSIOLOGICAL MEASURES or >Day 3 ☐				
Arterial line in situ?	Yes ☐ No ☐ If yes, report MAP			
Temperature °C	**Pre**	**Sit 10** ☐	**Stand** ☐	**Post**
MAP				
Systolic BP (mmHg)				
Diastolic BP (mmHg)				
Pulse rate (beats per min)				
O_2 Sats (%)				

Returned to rest after intervention to: ☐ Bed ☐ Chair

Borg perceived exertion score* ☐ ***Ask: How physically hard did you work?***

OR

Reason patient not mobilised for this session (tick one or more):
☐ Medically unwell ☐ Refused ☐ Pt not on ward ☐ No staff rostered/cover
☐ Other (comment) _____

AVERT DOSE Nurse Recording Form

Site #: ☐☐ Patient #: ☐☐☐ Patient Initials: ☐☐☐

Date of session: / / Session number: ☐

Start of session time: : (24 hour format)

Nurse Initials: ☐☐☐

Patient's functional level:

☐ Level 1 ☐ Level 2 ☐ Level 3 ☐ Level 4

At start of session, participant found in: ☐ Bed ☐ Chair

Provided by: ☐ No assist/Observed ☐ Nurse x1 ☐ Nurse x 2 ☐ PT x 1 ☐ PT x 2 ☐ Other Allied Health ☐ Health Care Assistant x 1 ☐ Student ☐ Family/Other

ENTER TIME IN MINS AT RELEVANT INTENSITY	
ACTIVITY/INTENSITY	**Time**
Hoist	
Lie to sit to lie	
Active sitting	
Sit to stand to sit	
Transfers	
Standing	
Early walking	
Walking	
Advanced walking	

Returned to rest after intervention to: ☐ Bed ☐ Chair

OR

Reason patient not mobilised for this session (tick one or more):

☐ Medically unwell ☐ Refused ☐ Pt not on ward ☐ No staff rostered/cover ☐ Other (comment) _____

Appendix C – Bedside Recording Form

Subject Nu☐☐☐☐☐ Subject Initials ☐☐☐	Date of Stroke: ☐☐ ☐☐☐ ☐☐☐☐ ☐

1. Insert the dates across the top row from the date of stroke.
2. Daily MSAS level to be entered.
3. Tick the days that the physiological measures will need to be taken. (First 3 days of PT training) Cross out days not required (weekends etc)
4. Tally of nursing sessions provided.

Date	Date of stroke																
Day post stroke	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
MSAS Level*																	
Physiological measures**																	
Nurse count																	

*To be reviewed each day and reassessed if required.
**Physiological measures to be taken at the first physiotherapy session of the day for the first 3 days of intervention provided. Weekends not required unless PT is provided.

References

1. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *British Medical Journal*. 2014;348:g1687
2. Borg GAV. Psychophysical bases of perceived exertion. *Medicine and Science in Sports and Exercise*. 1982;14:377-381
3. Walker MF, Hoffmann TC, Brady MC, Dean CM, Eng JJ, Farrin AJ, et al. Improving the development, monitoring and reporting of stroke rehabilitation research: Consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable. *Int J Stroke*. 2017;12:472-479