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Determining the optimal dose of reactive balance training after stroke – study protocol for a pilot randomized controlled trial

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1. ADMINISTRATIVE INFORMATION

Title: Determining the optimal dose of reactive balance training after stroke – study protocol for a pilot randomized controlled trial

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Contributorship: AM conceived of the study, is the grant holder, and drafted the manuscript. AM, ELI, and CJD developed the intervention. All authors contributed to study design, writing/editing the manuscript, and approved the final manuscript.

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2 26 **2. WHO DATASET**

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4 27 **1. Trial registration:** clinicaltrials.gov, NCT04219696

5
6 28 **2. Date of registration:** 7 January 2020

7
8 29 **3. Secondary identification numbers:** Not applicable

9
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11
12 Foundation Canadian Partnership for Stroke Recovery. AM holds a New Investigator Award
13 31
14 from the Canadian Institutes of Health Research (MSH-141983). We also acknowledge the
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17 33
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19 34
20 of Research and Innovation. These funding sources had no role in the design of this study and
21 35
22 will not have any role during its execution, analysis, interpretation of the data, or decision to
23 36
24 submit results.
25 37
26

27 38 **5. Primary sponsor:** Avril Mansfield

28
29 39 **6. Secondary sponsors:** Elizabeth Inness, Tanvi Bhatt

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32 2A2; tel: 416-597-3422 ext 7831; e-mail: avril.mansfield@uhn.ca

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34 42 **8. Contact for scientific queries:** Avril Mansfield; address: 550 University Ave, Toronto, ON,
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36 M5G 2A2; tel: 416-597-3422 ext 7831; e-mail: avril.mansfield@uhn.ca

37 43
38 44 **9. Public title:** Determining the optimal dose of reactive balance training after stroke

39 45 **10. Scientific title:** Determining the optimal dose of reactive balance training after stroke – a pilot
40
41 study
42 46

43 47 **11. Countries of recruitment:** Canada

44 48 **12. Interventions:** Reactive balance training. A research physiotherapist will oversee reactive
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46 balance training (RBT) in collaboration with participants' regular physiotherapists to ensure
47
48 consistent RBT delivery across participants. Training strategies will be individualized to each
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1
2 51 participant, based on their balance impairments and rehabilitation goals. The RBT program
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4 52 includes multi-directional 'internal' and 'external' balance perturbations. Internal perturbations
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6 53 are achieved by asking the participant to complete tasks that challenge balance control, such
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8
9 54 that they lose balance when attempting to perform the task (e.g., kicking a soccer ball). External
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11 55 perturbations are delivered manually using a push or pull from the physiotherapist. As
12
13 56 participants improve their reactive balance control, difficulty will be increased by shifting task
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15 57 requirements along a continuum from stable to mobile, and from predictable to unpredictable,
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18 58 and by increasing perturbation magnitude or imposing sensory or environmental challenges.

19
20 59 **13. Key inclusion and exclusion criteria:** Inclusion criteria: sub-acute stroke; receiving out-patient
21
22 60 rehabilitation at the Toronto Rehabilitation Institute; can stand independently for >30 seconds;
23
24
25 61 can walk with or without a gait aid (but without assistance of another person) for >10 metres;
26
27 62 and living in the community. Exclusion criteria: completed reactive balance training during in-
28
29 63 patient rehabilitation; lower-extremity amputation, weight-bearing restrictions, recent lower-
30
31 64 extremity injury or surgery (e.g., fracture), acute back or lower-limb pain, halo, aspen collar,
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33
34 65 history of fragility fracture and/or severe osteoporosis/osteopenia, contractures that prevent
35
36 66 neutral hip or ankle; activity restrictions following cardiac event/surgery, abnormal or unstable
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39 67 cardiovascular responses to exercise, arterial dissection; severe spasticity in the legs; cognitive
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41 68 impairment (i.e., unable to understand the purpose of training and/or to provide informed
42
43 69 consent); and/or acute illness (e.g., vomiting, fever), weight > 150 kg (exceeds safety harness
44
45 70 weight limits), colostomy bags, indwelling catheter, infection, pressure sore on pelvis or trunk.

46
47
48 71 **14. Study type:** Pilot parallel randomized controlled trial.

49
50 72 **15. Date of first enrolment:** February 2020 (anticipated).

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52 73 **16. Target sample size:** 36

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54 74 **17. Recruitment status:** Pending.

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57 75 **18. Primary outcome:** Rate of falls in daily life for six months post-discharge from rehabilitation.

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19. Secondary outcomes: Rate of accrual, rate of missing data, compliance with the intervention.

For peer review only

3. ABSTRACT

Introduction: Falls risk post-stroke is highest soon after discharge from rehabilitation. Reactive balance training (RBT) aims to improve control of reactions to prevent falling after a loss of balance. In healthy older adults, a single RBT session can lead to lasting improvements in reactive balance control and prevent falls in daily life. While increasing the dose of RBT does not appear to lead to additional benefit for healthy older adults, stroke survivors, who have more severely impaired balance control, may benefit from a higher RBT dose. Our long-term goal is to determine the optimal dose of RBT in people with sub-acute stroke. This assessor-blinded pilot randomized controlled trial aims to inform the design of a larger trial to address this long-term goal.

Methods and analysis: Participants (n=36) will be attending out-patient stroke rehabilitation, and will be randomly allocated to one of three groups: 1, 3, or 6 RBT sessions. RBT will replace a portion of participants' regular physiotherapy so that the total physical rehabilitation time will be the same for the 3 groups. Functional balance, balance confidence, and balance reactions will be assessed: 1) pre-training; 2) post-training; and 3) 6 months post-training. Participants will report falls and physical activity for 6 months post-discharge. Pilot data will be used to plan the larger trial (i.e., sample size estimate using fall rates, and which groups should be included based on between-group trends in pre-to-post training effect sizes for reactive balance control measures). Pilot data will also be used to assess the feasibility of the larger trial (i.e., based on the accrual rate, outcome completion rate, and feasibility of prescribing specific training doses).

Ethics and dissemination: Institutional research ethics approval has been received. Study participants will receive a lay summary of results. We will also publish our findings in a peer-reviewed journal.

4. STRENGTHS AND LIMITATIONS

- The intervention will replace a portion of participants routine physiotherapy during out-patient rehabilitation. Therefore, the findings will be directly relevant to clinical practice.
- Conversely, there is a risk that many patients will decline participation in the study as they will not want their rehabilitation care to be disrupted.
- This is a pilot study, so it is unlikely that we will be able to make definitive decisions regarding the optimal dose of reactive balance training post-stroke.

5. INTRODUCTION

5.1 Background and rationale

Falls are the most prevalent complications during all stages of stroke recovery.¹ Along with physical injuries, 88% of people with stroke who fall develop fear of falling.² Falls and fear of falling can lead to inactivity, deconditioning, and lower functional capacity, further increasing fall risk^{3,4} and reducing quality of life.⁵

Conventional balance training reduces falls in older adults,⁶ but not after stroke.^{7,8} Reactive balance training (RBT), where clients experience repeated postural perturbations (or loss of balance),^{9,10} is a novel type of exercise that aims to improve reactive balance control. RBT can prevent falls in older adults and people with Parkinson's disease.¹¹ Our non-randomized study suggests that RBT reduces fall rates after discharge from stroke rehabilitation.¹² In our previous study, the intervention was implemented as part of routine care, and the dose of RBT depended on client goals and preferences and length of stay, rather than being prescribed by the study protocol. Participants completed 1-12, 30-minute RBT sessions (median of 6 sessions).¹²

Unlike other forms of exercise,¹³ improved reactive balance control with RBT seems to occur with few repetitions, and is maintained for several months without training. Among healthy older adults, just 24 perturbations within a single session of RBT is sufficient to lead to lasting improvements (i.e., 6-12 months) in reactive balance control,¹⁴ and prevent falls in daily life.¹⁵ One study in people with chronic stroke found that improved reactive balance control with a single session of RBT was retained for 3 weeks post-training.¹⁶ While almost doubling the dose of RBT does not appear to lead to additional benefit for healthy older adults,¹⁷ it is possible that those with stroke would benefit from additional RBT as they have more severely impaired balance than healthy older adults.¹⁸ Additional training may also promote sustained training effects beyond 3 weeks.¹⁹ Only two previous studies have investigated RBT in sub-acute stroke.^{12,20} This is a crucial period for fall prevention due to the high risk

1
2 133 of falls early after stroke.²¹ Therefore, there is a need to establish optimal RBT training parameters in
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4 134 the sub-acute stroke population.
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6 7 135 8 9 136 **5.2 Objectives and research questions**

10
11 137 The long-term goal of this work is *to determine the optimal dose of RBT in people with sub-acute*
12
13 138 *stroke*. This assessor-blinded pilot randomized controlled trial (RCT) aims *to inform the design of a*
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15
16 139 *larger trial to address this long-term goal*. Specifically, the following questions about the larger trial
17
18 140 will be answered with this pilot study:

- 19
20 141 1) what is the optimal sample size;
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22 142 2) how long will it take to achieve this sample size;
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24 143 3) what secondary outcome measures should be used;
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26 144 4) how feasible is it to prescribe a specific dose of RBT to people with sub-acute stroke; and
- 27
28 145 5) what two intervention groups should be included in the larger trial?
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32 146 33 34 147 **5.3 Trial design**

35
36 148 This is an assessor-blinded pilot RCT (Figure 1). People who are attending out-patient stroke
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38
39 149 rehabilitation will be randomly assigned to one of three different doses of reactive balance training
40
41 150 (RBT). Reactive balance control, functional balance, and balance confidence will be measured pre- and
42
43 151 post-training and 6 months post-training. Falls in daily life, physical activity, and participation will be
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45
46 152 assessed for 6 months post-training.
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48 153 49 50 154 *5.3.1 Patient and public involvement*

51
52 155 This study was designed without patient involvement. Patients were not invited to comment on the
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54
55 156 study design and were not consulted to develop patient relevant outcomes. Some trial design elements
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1
2 157 were informed by participant feedback from our previous RBT study.¹⁹ Patients were not invited to
3
4 158 contribute to the writing or editing of this document for readability or accuracy.
5

6 159 7 8 9 160 **6. METHODS: PARTICIPANTS, INTERVENTIONS, AND OUTCOMES** 10

11 161 **6.1 Study setting** 12

13 162 This study will take place at the Toronto Rehabilitation Institute, University Health Network. This
14
15
16 163 facility provides specialized in- and out-patient stroke rehabilitation to individuals in the sub-acute
17
18 164 stage of stroke recovery. Out-patient stroke rehabilitation at the Toronto Rehabilitation Institute
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20 165 typically includes 45 minutes of physiotherapy 2-5 times/week for at least 4 weeks.
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23 166 24 25 167 **6.2 Participants** 26

27 168 Participants will be people with sub-acute stroke (<6-months post-stroke) who are receiving out-patient
28
29 169 rehabilitation at the Toronto Rehabilitation Institute. Participants will be eligible if they can: 1) stand
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31
32 170 independently for >30s; 2) walk with or without a gait aid (but without assistance of another person)
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34 171 for >10m; and 3) are living in the community. Participants will be excluded if they have:
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- 36 172 • Completed RBT during in-patient rehabilitation;
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38
39 173 • Lower extremity amputation, weight-bearing restrictions, recent lower-extremity injury or
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41 174 surgery (e.g., fracture), acute back or lower-limb pain, halo, aspen collar, history of fragility
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43 175 fracture and/or severe osteoporosis/osteopenia, contractures that prevent neutral hip or ankle;
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45
46 176 • Activity restrictions following cardiac event/surgery, abnormal or unstable cardiovascular
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48 177 responses to exercise, arterial dissection;
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51 178 • Severe spasticity in the legs;
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53 179 • Cognitive impairment (i.e., unable to understand the purpose of training and/or to provide
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55 180 informed consent), as determined by the healthcare team; and/or
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- Acute illness (e.g., vomiting, fever), extreme obesity (exceeds safety harness system weight limits), colostomy bags, indwelling catheter, infection, pressure sore on pelvis or trunk.

After participants provide consent, eligibility will be confirmed using information in the participants' hospital chart, by consulting members of the patient's healthcare team, and by consulting the participant themselves. Participants will still receive their usual care, while participating in the study.

Participants will be informed that they are free to withdraw from the study at any time point, without consequence. If participants ask to be withdrawn from the study, any data collected from them up to that point will be used to answer the research questions. Participants may also be withdrawn from the study due to changes in their health status that affect eligibility.

6.3 Interventions

Participants will be allocated to one of three groups: one, three, or six, 45-minute RBT sessions. RBT will replace a portion of participants' regular physiotherapy, so that the total amount of physical rehabilitation will not be affected by study participation, and will be approximately equal for the three groups. Each 45-minute session will be entirely dedicated to RBT, and will include up to 60 perturbations. The proposed session duration and number of perturbations per session is double that of our previous sub-acute study, whereas the number of sessions is halved.¹² This previous study was conducted during in-patient rehabilitation, where patients are typically provided with 60-minutes of physiotherapy 5 days per week. Within this schedule, patients could easily complete 30 minutes of RBT, leaving 30 minutes per day for other physical therapies. However, as out-patient physiotherapy is only 45 minutes per session, the proposed dosages more easily fit into most out-patient rehabilitation therapy schedules.

A research physiotherapist will oversee RBT in collaboration with participants' regular physiotherapists to ensure consistent RBT delivery across participants. Training strategies will be individualized to each participant, based on their balance impairments and rehabilitation goals.^{12,19} The

1
2 206 RBT program includes multi-directional ‘internal’ and ‘external’ balance perturbations. Internal
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4 207 perturbations are achieved by asking the participant to complete tasks that challenge balance control,
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6 208 such that they lose balance when attempting to perform the task (e.g., kicking a soccer ball). External
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9 209 perturbations are delivered manually using a push or pull from the physiotherapist. As participants
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11 210 improve their reactive balance control, difficulty will be increased by shifting task requirements along a
12
13 211 continuum from stable to mobile, and from predictable to unpredictable, and by increasing perturbation
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16 212 magnitude or imposing sensory or environmental challenges.²²
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20 214 **6.4 Outcome measures**

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23 215 To assess feasibility of the study, we will document rates of accrual (i.e., number of patients
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25 216 approached to participate in the study versus the number who provide consent), number of training
26
27 217 sessions attended/missed, reasons for missed sessions, and rate of missing data for the outcomes
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29
30 218 described below.

31
32 219 Table 1 summarizes additional outcome measures. Demographic, stroke information, and
33
34 220 medical history will be extracted from participants’ hospital charts. Participants will complete a
35
36 221 questionnaire at baseline that asks about their social supports, employment, familial responsibilities,
37
38
39 222 living situation etc., which are factors that could influence fall risk. Many of these questions have been
40
41 223 adapted from the Canadian Longitudinal Study on Aging.²³ The National Institutes of Health Stroke
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43 224 Scale (NIH-SS)²⁴ will be scored at study enrolment. Clinical assessments will be scored by a blinded
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45
46 225 research assistant at three time points: 1) pre-training; 2) post-training; and 3) 6 months post-training.
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48 226 Tests will include: Chedoke-McMaster Stroke Assessment (CMSA)²⁵ foot and leg scores; mini-
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50 227 Balance Evaluation Systems Test (mini-BEST);²⁶ Activities-specific Balance Confidence (ABC)
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52
53 228 scale;²⁷ and reactive balance control following unpredictable and novel perturbations.

54
55 229 To assess reactive balance control, participants will be outfitted with reflective markers, and
56
57 230 will complete 8-10 walking trials on a movable platform. There will be four force plates embedded in
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1
2 231 the movable platform. On two trials, the platform will move forward suddenly on heel strike (i.e., when
3
4 232 one of the force plates is loaded) to trigger a slip-like perturbation.²⁸ On two other trials, the platform
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6 233 will move backward suddenly on toe-off (i.e., when one of the force plates is unloaded) to trigger a
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8
9 234 trip-like perturbation. The perturbation waveform will consist of a 300 ms square-wave acceleration,
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11 235 followed immediately by 300 ms deceleration (peak acceleration up to 1.5m/s²).²⁸ The platform will
12
13 236 only move during these four trials, such that the perturbation will be unpredictable to participants.
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16 237 These perturbations differ from what will be used during training, and will measure transfer of training
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18 238 to a novel and ecological loss of balance. Three-dimensional motion capture will record the locations of
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20 239 the reflective markers in space. Biomechanical stability when responding to the perturbation will be
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22 240 measured using an established method that considers the distance between the centre of mass and base
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24
25 241 of support;^{28,29} in general, a more posteriorly- (slip) or anteriorly-located (trip) centre of mass in
26
27 242 relation to the perturbed lower limb is considered less stable.

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30 243 Participants will be asked to report falls (“an event that results in a person coming to rest
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32 244 unintentionally on the ground or other lower level”³⁰) in the 6 months post-training. Participants will be
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34 245 provided with stamped, addressed postcards to mail to the research team every 2 weeks for 6 months
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36 246 post-training. Postcards will contain a calendar, on which participants will record falls. The blinded
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38
39 247 research assistant will call participants who do not return the postcard to determine if any falls
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41 248 occurred. The research assistant will contact participants reporting a fall to complete a short
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43 249 questionnaire determining the cause and consequences of the fall. This method is considered the ‘gold
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45 250 standard’ for fall reporting.³¹

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48 251 Participants will also report physical activities using the Physical Activity Scale for Individuals
49
50 252 with Physical Disabilities (PASIPD),³² and participation in daily life using the Subjective Index of
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52 253 Physical and Social Outcome (SIPSO) at 2-, 4- and 6-months post-discharge.
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56 57 255 **6.5 Sample size**

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1
2 256 We will aim to recruit 12 participants per group (36 participants total), as recommended for pilot
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4 257 studies.³³
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6 258 7 8 9 259 **6.6 Recruitment**

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11 260 Participants will be recruited from the Toronto Rehabilitation Institute University Centre out-patient
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13 261 stroke rehabilitation program. This program admits approximately 200 individuals with stroke per year.
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16 262 Potentially eligible participants will be identified by the patients' primary treating physiotherapist.
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18 263 Participants will be reimbursed for any travel expenses (e.g., public transit, taxi, or parking) they incur
19
20 264 to attend data collection appointments; participants will not be reimbursed for travel expenses for the
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22 265 intervention as they were occur as part of routine care. Participants will also receive a \$50 gift card
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24
25 266 upon completion of the study as a modest incentive to participate.
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27 267 28 29 268 **7. METHODS: ASSIGNMENT OF INTERVENTIONS**

30 269 **7.1 Group allocation**

31
32 270 Participants will be assigned using blocked randomization to one of the three different doses of RBT
33
34 271 (block size: 6). The random allocation sequence will be computer generated. Blocked randomization
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37 272 will ensure equal numbers allocated to each group. Group allocation will be performed centrally by the
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39 273 principal investigator, who will not be involved in recruiting, scoring assessments, or administering the
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41 274 interventions (i.e., concealed allocation).
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45 46 276 **7.2 Blinding**

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48 277 Outcome measures will be obtained by a research assistant who will be blinded to group allocation. At
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50 278 the post-training and follow-up study visits, the research assistant will be asked to guess the
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53 279 participants' group allocation, and if the research assistant received any information about participant
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55 280 group allocation that led to unblinding. Participants cannot be blinded to group allocation.
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8. METHODS: DATA COLLECTION, MANAGEMENT, AND ANALYSIS

8.1 Data collection methods

Data will be collected primarily by the research assistant either directly from the participant or by chart review (see Table 1 for further details). The research assistant will receive training regarding data collection from the principal investigator (AM). Questionnaires will be completed via in person interview at enrolment, and over the telephone at the follow-up time points.

8.2 Data management

Electronic data will be stored on secure institutional servers. Hard copies of files containing de-identified data will be stored in locked cabinets and/or in offices that are locked when not occupied.

8.3 Data analysis

Data analysis will address the research questions as described below.

1. *What is the optimal sample size?* The primary outcome in the larger trial will be rate of falls in daily life. The rate of falls (number of falls per person-year) in the one-session group, and a clinically meaningful 30% reduction in fall rates, will be used to estimate sample size for the larger trial.³⁴
2. *How long will it take to achieve this sample size?* We will use the accrual rate from the pilot study (number of participants recruited per month) to estimate how long it will take to achieve the target sample size in the larger trial.
3. *What secondary outcome measures should be used?* Our previous work supports feasibility of data collection using most of the measures in this population.¹² However, we have not previously tested the slip- and trip-like perturbations in this population. We will examine between-group effect sizes for this test to determine if it is useful for revealing training effects. We will also report on

1
2 306 completeness of data collection for this, and other, outcome measures; the larger trial will only
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4 307 include outcomes with $\geq 80\%$ completion rate.
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- 6 308 4. *How feasible is it to prescribe specific dose of RBT to people with sub-acute stroke?* The feasibility
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8 of prescribing a specific RBT dose during patients' routine rehabilitation is not known. The dose
9 309 will be considered feasible if the mean number of sessions and number of perturbations per session
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11 310 is $\geq 75\%$ of prescribed.
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13 311
14
15 312 5. *What two intervention groups should be included in the larger trial?* We will use the reactive
16
17 control sub-scale of the mini-BEST as a measure of effect of RBT on reactive balance control in
18 313 each group. Scores on this sub-scale have been shown to improve with a high dose of RBT in
19
20 314 people with chronic stroke.¹⁹ We will calculate the pre-to-post training effect sizes for this sub-
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22 315 scale for each group (i.e., mean difference in the score from pre-training to post-training). The
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24 316 minimum detectable change for the total mini-BEST score in people with stroke is 3 points³⁵ (i.e.,
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26 317 $\sim 10\%$ of the maximum score). The minimum detectable change for individual sub-scales have not
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28 318 been established, but we will assume that this is 10% of the maximum score for the subscale (i.e.,
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30 319 0.6 points). Therefore, if the pre-to-post training effect sizes are within 0.6 points for the three-
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32 320 session and six-session groups, then the larger trial will include the one-session and three-session
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34 321 groups. However, if effect sizes reveal a trend towards greater improvement for the six-session
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36 322 group, then the larger trial will include the one-session and six-session groups.
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45 325 Data will be analyzed at the end of the study. Therefore, there is no plan for interim analyses of
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47 primary and/or secondary variables.
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50 327 51 52 328 **9. METHODS: MONITORING**

53 329 **9.1 Data monitoring**

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2 330 There is no data monitoring committee for this study; several previous studies have already
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4 331 demonstrated that reactive balance training is safe for people with stroke, with few adverse events
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6 332 reported.^{12,16,19,20} Adverse events that meet all three of the following criteria will be reported
7
8
9 333 immediately to the institution's Research Ethics Board, as is routine practice: 1) unexpected in terms of
10
11 334 nature, severity, or frequency; 2) related or possibly related to participation in the research; and 3)
12
13 335 suggests a potential increased in risk of harm to research participants or others. All adverse events will
14
15
16 336 be collated and evaluated bi-annually by the principal investigator (AM).
17
18 337
19

20 338 **9.2 Potential harms**

21
22 339 In a previous study, mild adverse events related to RBT in people with stroke were delayed-onset
23
24 340 muscle soreness, fatigue, or exacerbation of joint pain (11%, 7%, and 32% of participants,
25
26 341 respectively),¹⁹ which did not require medical attention, but resulted in reduced intervention intensity
27
28 342 until they resolved (typically by the following session). Of note, the frequency and severity of adverse
29
30 343 events are similar for the RBT group and control group, who completed more 'traditional' balance
31
32 344 training.¹⁹ Therefore, these types of adverse events are typical of similar exercise programs, and not
33
34 345 specific to RBT.
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39 346 As the assessment and intervention includes tasks that are deliberately challenging to balance
40
41 347 control, there is a small risk that participants, upon loss of balance, will fall. Appropriate precautions
42
43 348 will be taken to ensure patient safety during these tasks. Interventions will be administered by a trained
44
45 349 and licensed physiotherapist who will tailor the training to the patient's abilities. Assessments will be
46
47
48 350 completed by a trained research assistant with a health sciences background. A safety harness attached
49
50 351 to a secure point overhead will be worn for all postural perturbations to prevent a fall to the floor if the
51
52 352 individual fails to regain stability. Additionally, the research assistant or physiotherapist can provide
53
54
55 353 assistance to prevent a fall. We have administered tens of thousands of postural perturbations to over
56
57 354 500 individuals with varying balance abilities in previous research studies and clinical activities and no
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1
2 355 participant suffered an injury as a result of an induced postural perturbation. However, even if the
3
4 356 participant is caught by the safety harness or researcher, there is a very small chance that participants
5
6 357 will suffer a physical injury (e.g., sprain or bruise). In the event of a minor physical injury, the
7
8
9 358 physiotherapist will provide first aid, will advise the participant regarding follow-up with a medical
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11 359 professional (e.g., family doctor) and home treatment (e.g., rest, ice, compression, elevation), and will
12
13 360 follow-up with the participant after a day or two.

15
16 361 The physiotherapist will communicate regularly with the participant's care team about changes
17
18 362 in health status that could affect risk profile. Participants will be withdrawn if their health changes such
19
20 363 that they would no longer be eligible for the study (i.e., one of the exclusion criteria applies to them).
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23 364

25 365 **10. ETHICS AND DISSEMINATION**

27 366 **10.1 Research ethics approval**

29
30 367 Research ethics approval has been received by the Research Ethics Board of the University Health
31
32 368 Network (Study ID: 19-6001, approved 17 January 2020).
33

36 370 **10.2 Protocol amendments**

38
39 371 Substantive changes to the design or conduct of the study will require a formal amendment to the study
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41 372 protocol. Such substantive amendments will be agreed upon by the study investigators and will be
42
43 373 approved by the Research Ethics Board of the University Health Network prior to implementation.
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45 374 Minor administrative changes to study documents (e.g., correcting a typographical error or clarifying a
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48 375 questionnaire item) may also be implemented, with the Research Ethics Board notified of the changes.
49

52 377 **10.3 Consent**

54
55 378 Potentially eligible participants will be identified by the patients' primary treating physiotherapist. The
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57 379 physiotherapist will ask patients if they are interested in speaking with a research assistant regarding
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1
2 380 the study. If patients agree, they will be approached by a member of the research team (DJ, CJD or a
3
4 381 delegate acting on their behalf) who will explain the study and provide patients with the study
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6 382 information sheet and consent form (Appendix). Research personnel will answer the patient's questions
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8
9 383 about the study. Patients may discuss the study with their friends, family members, or healthcare
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11 384 providers. Patients may take as long as necessary to decide if they wish to participate in the study;
12
13 385 however, if a patient has not decided before they are discharged then we will assume they have
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15
16 386 declined participation. The informed consent process will be documented by research personnel.
17

18 387 19 20 388 **10.4 Confidentiality**

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22 389 Personal information is any information that could identify participants. If participants agree to join this
23
24
25 390 study, the following personal information will only be accessible to the research team, for contact
26
27 391 purposes: name, telephone number, mailing address, and e-mail address (if provided). A number of
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29 392 steps will be taken to ensure protection of personal health information. All information collected during
30
31
32 393 this study, including the participant's personal information, will be kept confidential and will not be
33
34 394 shared with anyone outside the study unless required by law. Electronic data will be stored on secure
35
36 395 servers for 10 years. After 10 years the data will be deleted from the servers. Electronic files containing
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39 396 patient names and contact information will be password protected, and will be stored separately from
40
41 397 study data. Hard copies of files containing de-identified data will be stored in locked cabinets and/or in
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43 398 offices that are locked when not occupied. Consent forms will be stored in locked cabinets/offices
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46 399 separately from other data. Only those individuals who require access to the data for the purpose of this
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48 400 study will be provided with the password to the file containing identifiers and/or the keys to the locked
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50 401 cabinet/office.
51

52 402 53 54 55 403 **10.5 Declaration of interests**

56
57 404 The authors declare that they have no competing interests related to this study.
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10.6 Access to data

The principal investigator (AM) will have access to the full dataset. There is no current plan to make the participant-level dataset available publicly; however, the dataset may be made available in future via a Data Access Committee, if such a committee is established by the institution.

10.7 Ancillary and post-trial care

The University Health Network will be responsible for providing out-of-pocket expenses to ensure that a participant receives immediate medical care in the event that the participant experiences an adverse health event (e.g., injury) as a result of participation in the study. Patients do not typically receive follow-up after discharge from rehabilitation; therefore, there is no plan for any post-trial care.

10.8 Dissemination policy

Participants will receive a letter of appreciation at the end of the study, which may include a brief summary of the study results. Study results will be shared with the academic community via publication in peer-reviewed journals and presentations at conferences. We will aim to submit a paper describing analysis of the primary and secondary outcomes within 6 months of completing data collection. All individuals who meet the International Committee of Medical Journal Editors criteria for authorship will be included as authors on any publications arising from this work. We will share results directly with physiotherapists through interactive workshops (e.g., at the Canadian Physiotherapy Association meeting). We are developing a toolkit to assist physiotherapists implementing RBT. The results of the larger trial will be incorporated into the toolkit as recommendations for RBT dose in sub-acute stroke.

11. SIGNIFICANCE

1
2 430 A high rate of falling is a common after stroke, and fall risk is highest in the first months post-discharge
3
4 431 from rehabilitation.²¹ RBT is a novel type of exercise that aims to improve reactive balance control,
5
6 432 rather than 'traditional' balance training, which focuses on maintaining stability during voluntary
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9 433 movement. Time in stroke rehabilitation is limited, and physiotherapists report lack of time is a barrier
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11 434 to implementing RBT.³⁶ The results of the proposed study will inform the design of a larger RCT to
12
13 435 establish the optimal dose of RBT in sub-acute stroke. If a low dose of RBT can improve reactive
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16 436 balance control and prevent falls post-stroke, this would allow therapists and patients to more easily
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18 437 include this fall-prevention intervention in rehabilitation, without sacrificing time spent working on
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20 438 other important rehabilitation goals.
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13. TABLES

Table 1: Cohort descriptors and outcome measures.

	Pre-training	Post-training	6-month follow-up
Demographics	✓		
Time post-stroke	✓		
Lesion location	✓		
Medical history	✓		
Medications	✓		
Changes in health/medications		✓	✓
NIH stroke scale ²⁴	✓		
Chedoke McMaster Stroke Assessment ²⁵	✓	✓	✓
Mini-Balance Evaluation Systems Test ²⁶	✓	✓	✓
Activities-specific Balance Confidence scale ²⁷	✓	✓	✓
Novel unpredictable perturbation	✓	✓	✓
Falls in daily life			✓*
Physical Activity Scale for Individuals with Physical Disabilities ³²			✓*
Subjective Index of Physical and Social Outcome ³⁷			✓*

*Data collected repeatedly during the 6-month follow-up period.

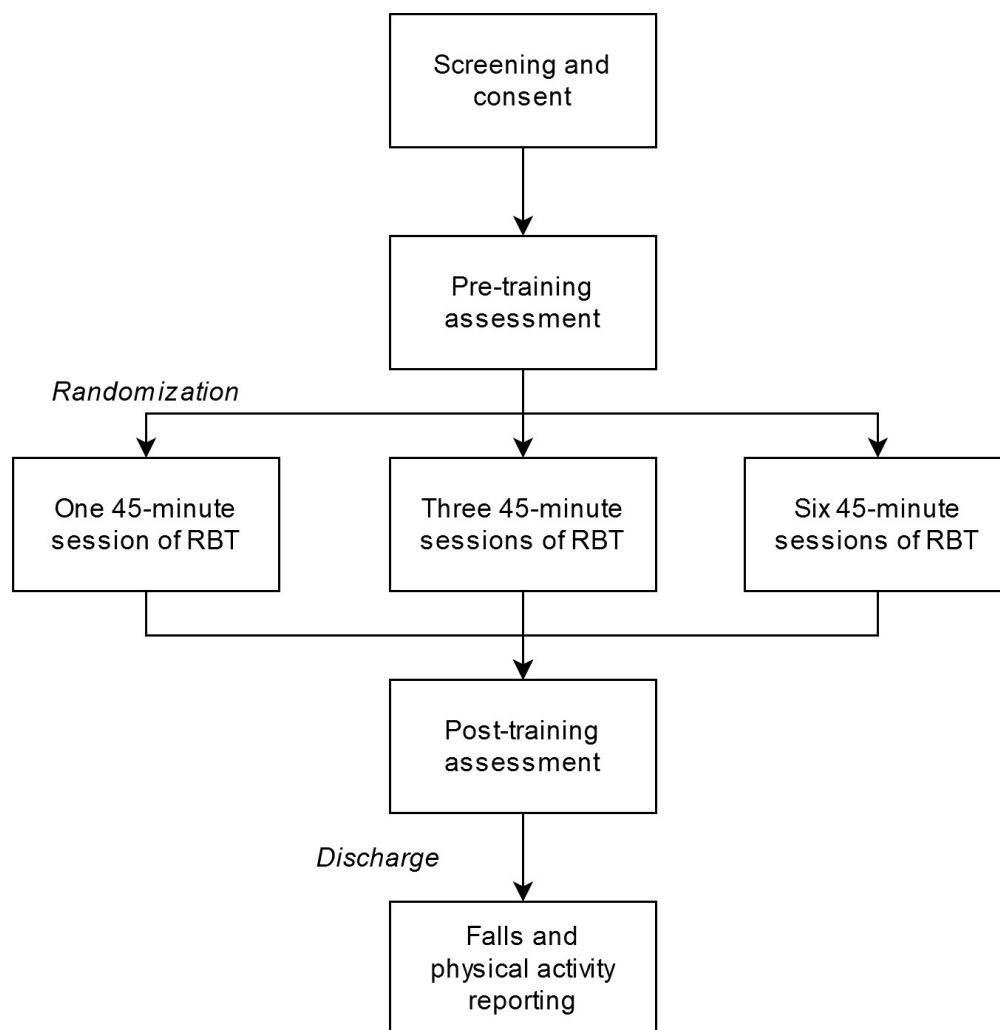
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2 538 **14. FIGURE CAPTIONS**

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4 539 **Figure 1: Trial design.**

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For peer review only



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Figure 1: Trial design.

477x487mm (72 x 72 DPI)



CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Study title: Determining the optimal dose of reactive balance training after stroke □a pilot study

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*Please note that communication via e-mail is not absolutely secure. Thus, please do not communicate personal sensitive information via e-mail.

Funding

This study is funded by the Heart and Stroke Foundation Canadian Partnership for Stroke Recovery.

IMPORTANT: You are being invited to take part in a research study. Before you agree to take part, it is important that you read the information below. The information describes the purpose of the study, the risks or benefits to you, and your right to withdraw at any time. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish including your friends, family, and family doctor. Participation in this study is voluntary.

Objective of the study

People who have had a stroke tend to fall more often than those who have not had a stroke. A reactive balance training program might help reduce fall rates after discharge from stroke rehabilitation. Some studies suggest that people can benefit from even small amounts of reactive balance training, but we do not know how much reactive balance training is necessary to improve balance and prevent falls. Our long-term goal is to determine the ideal number of reactive balance training sessions that will improve reactive balance control and prevent falls. We are currently conducting a small pilot study to determine the feasibility of a larger study to address this long-term goal.

You are being asked to participate because you have had a stroke within the last 6 months, you are attending outpatient rehabilitation at Toronto Rehab, and you are able to walk without assistance of another person.

Up to 36 people will participate in this study and it will take approximately 18 months to recruit all participants.

Study visits and procedures

If you agree to participate in the study, we will review your chart, you will complete balance training, we will test your balance and function, and we will ask you to report falls. The parts of the study are described below.

Chart review

We will review your hospital chart to get some information about your stroke, your previous medical history, and your current prescription medications. We use this information to confirm that you are eligible for the study and to describe the type of people who have participated in the study. You do not need to do anything additional for the chart review.

Reactive balance training

Reactive balance is the kind of balance that you need to stop yourself from falling after you stumble, trip, or get bumped, or jostled. Reactive balance requires you to step very quickly when you have lost your balance, to prevent a fall. In order for you to re-learn reactive balance, you need to lose your balance so that you can practice recovering with rapid steps. This is called **reactive balance training**.

Reactive balance training will be completed by your physiotherapist, and/or by a research physiotherapist. Reactive balance training is done in a safe, supportive, supervised environment. You will wear a harness which is attached to an overhead frame. The harness is worn so that when you lose your balance, you do not risk falling all the way to the floor. The physiotherapist will be there as well to assist you should you be unable to recover your balance on your own.

1
2 The physiotherapist will ask you to do exercises that cause you to lose your
3 balance. He or she will do this in one of two ways:

- 4 1. he or she will have you practice tasks that gradually challenge your balance
5 and result in a loss of balance, or
- 6 2. he or she will gradually pull or push you until you lose your balance.
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14 Images removed for publication
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20 **Example of task to challenge balance:** tapping
21 on unstable surfaces with alternating feet
22

23
24 **Example of 'pull' by
25 physiotherapist to left**

26 You will receive 1, 3, or 6 reactive balance training sessions; each session will be
27 45-minutes long and will replace 1, 3, or 6 of your regular physiotherapy
28 sessions. The timing of the sessions during your outpatient rehabilitation will be
29 determined by your physiotherapist.

30 Balance and functional testing

31 You will be asked to complete three testing sessions: 1) just before you start the
32 reactive balance training; 2) at the time of discharge from rehab; and, 3) 6-
33 months after you finish the training. Each testing session will last 2-2.5 hours.
34 The first session will be longer than the other two. You can take rest breaks as
35 often as you need during the testing sessions. During these test sessions, we will
36 ask you several questions and conduct several tests.
37
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- 39
40 Information about you (10 minutes) we ask you some questions about
41 you and your life. We will ask questions about your employment, education
42 history, and social networks. We use this information to describe the type of
43 people who have participated in this study.
44
45
46 Stroke function tests (20 minutes, first visit only) - we will do some quick
47 tests of your vision, memory, sense of touch, and arm and leg function.
48 These tests tell us how your stroke has affected you. We use this
49 information to describe the kind of people who participate in the study.
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51
52 Questionnaire (10 minutes) - we will ask you to complete a standardized
53 questionnaire about your balance confidence. We would like to know if
54 balance confidence improves after completing the training. You are free to
55 choose not to answer any of the questions. You can take the questionnaire
56 away with you and answer it at home if you like.
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3 Leg and foot recovery (10 minutes) we will ask you to do a few
4 movements with your leg and foot that have been affected by the stroke,
5 such as bending the knee or wiggling the toes. We would like to know if
6 your ability to move the leg and foot improves after completing the training.
7
8
9 Balance test (15 minutes) - we will ask you to do several activities that
10 challenge your balance and mobility, such as walking as quickly as you can,
11 standing with your eyes closed, and recovering your balance once released
12 from a leaning position. A research assistant will stand near you when you
13 complete the tests to provide any assistance you might need. The research
14 assistant will rate how you perform on each test. We would like to know if
15 your ability to perform these tests improves after completing the training.
16
17
18 Balance reaction test (1 hour) - we will test your balance reactions on a
19 movable platform. During this test, you will wear a safety harness attached
20 to an overhead beam and you will be outfitted with reflective markers. We
21 will ask you to walk forward on the platform 8-10 times. During 2 of the
22 walking trials, the platform will move suddenly, requiring you to react to
23 regain your balance. If you are unable to use your own balance reactions to
24 prevent a fall, the safety harness will catch you. We would like to know if
25 your balance reactions improve after completing the exercise program.
26 Setting up for this test takes quite a bit of time, but the tests themselves
27 will only take about 10-15 minutes.
28
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32 All of the balance tests will be videotaped so that we can check out you
33 performed the tests after you finish your appointment. The videotaping is
34 mandatory for the study. Only study personnel will have access to your video
35 images. We may ask for your permission to show the videos to some people
36 outside the study (e.g., for educational purposes). We will ask you to provide this
37 permission by signing a separate consent form, but you do not have to provide
38 this permission. We will not share the videos with anyone outside of the study
39 without your permission.
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43 Falls reporting

44 We will ask you to complete a six-month falls monitoring period. When you have
45 completed the assessment at the end of rehabilitation you will be provided with a
46 calendar that you will be asked to fill out daily. You will use this calendar to
47 record any falls or near falls that you experience. We will ask you to return the
48 calendar to us every two weeks. If you experience a fall or a near fall, it is
49 important that you get the medical care you may need. After your medical care is
50 addressed, we will ask you (or a family member) to contact us to answer some
51 questions about the fall or near fall. You can answer these questions over the
52 telephone. The questions include what you were doing when you fell, what you
53 think caused the fall, and whether you have a fear of falling. The questions should
54 take 15-30 minutes to answer.
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1
2 If you agree to participate in this study you will have to fill out the falls
3 monitoring calendar every day and return it to us every two weeks. We will also
4 call you frequently to ask you questions about your falls and physical activities.
5 You might find that the calendars and the phone calls are inconvenient.
6
7

8 If you have difficulty understanding or speaking English you may need a family
9 member or friend to help you to participate in this study. They may need to
10 translate some of the study documents and questionnaires, speak to our research
11 personnel on the telephone. This may inconvenience your family member or
12 friend.
13
14

15 **Potential benefits**

16 If you participate in this study you will participate in reactive balance training. It
17 is possible that this training will benefit your balance.
18
19

20 The results of this study will give us more information about the amount of
21 training that is required to improve balance reaction. These results will be used to
22 inform the next research study and could be used in rehabilitation programs and
23 benefit other stroke patients in the future.
24
25

26 **Reminders and responsibilities**

27 It is important to remember the following things during the study:

- 28 Tell the study staff your health history and medications as accurately as
29 possible. This will help to prevent any harm to you.
- 30 Ask the study staff about anything that worries you.
- 31 Tell the study staff if anything about your health has changed.
- 32 Return the falls calendars regularly and report any falls to the study staff as
33 soon as possible.
34
35
36

37 **Alternatives to being in a study**

38 You do not have to join this study to receive treatment for your stroke. Your
39 outpatient rehabilitation program will be provided as scheduled.
40
41

42 **Confidentiality**

43 Your data will be shared as described in this consent form or as required by law.
44 All personal information such as your name, address, and phone number will be
45 removed from the data and will be replaced with a number. A list linking the
46 number with your name will be kept by the study investigator in a secure place,
47 separate from your file.
48
49

50 **Personal Health Information**

51 If you agree to join this study, the research team will look at your personal health
52 information and collect only the information they need for the study. Personal
53 health information is any information that could identify you and includes your:

- 54 name,
- 55 address,
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1
2 x age, and,
3 new or existing medical records, that includes types, dates and results of
4 medical tests or procedures.
5

6
7 Representatives of the University Health Network (UHN) including the UHN
8 Research Ethics Board may look at the study records and at your personal health
9 information to check that the information collected for the study is correct and to
10 make sure the study is following proper laws and guidelines.
11

12
13 The research team will keep any personal health information about you, including
14 the videos, in a secure and confidential location for 10 years after we have
15 finished collecting data for this study. All information collected during this study,
16 including your personal health information, will be kept confidential and will not
17 be shared with anyone outside the study unless required by law. You will not be
18 named in any reports, publications, or presentations that may come from this
19 study.
20
21

22 *Research information in shared clinical records*

23 If you participate in this study, information about you from this research project may be stored
24 in your hospital file and in the UHN computer system. The UHN shares the patient information
25 stored on its computers with other hospitals and health care providers in Ontario so they can
26 access the information if it is needed for your clinical care. The study team can tell you what
27 information about you will be stored electronically and may be shared outside of the UHN. If
28 you have any concerns about this, or have any questions, please contact the UHN Privacy
29 Office at 416-340-4800, x6937 (or by email at privacy@uhn.ca).
30
31
32

33 **Alternatives to being in the study**

34 The usual treatment for people with stroke at Toronto Rehab includes the
35 treatment of balance when indicated. Your treatment will include all regular
36 therapy programs as well as the addition of reactive balance training sessions.
37
38

39 **Voluntary participation**

40 You are encouraged to ask any questions that you may have about this study. If
41 you do not wish to participate in this study it will not affect any treatment that
42 might receive at Toronto Rehab or the University Health Network in the future. If
43 you chose to participate initially but wish to withdraw at a later date, for any
44 reason, it will not affect any future care that you receive at Toronto Rehab or the
45 University Health Network. We will give you any new information about the study
46 that might affect your decision to stay in the study.
47
48
49

50 **Withdrawal from the study**

51 If you choose to leave the study, the information that was collected before you
52 left the study will still be used in order to help answer the research question. No
53 new information will be collected without your permission.
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Costs and reimbursement

You will be reimbursed for any travel expenses that result from the follow-up appointments. These travel expenses may include TTC fare, taxi fare, or parking. You will receive a \$50 gift card upon completion of the study.

Rights as a participant

If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.

By signing this form you do not give up any of your legal rights against the investigators, sponsor or involved institutions for compensation, nor does this form relieve the investigators, sponsor or involved institutions of their legal and professional responsibilities.

Conflict of interest

Researchers have an interest in completing this study. Their interests should not influence your decision to participate in this study.

Questions about the study

If you have any questions, concerns or would like to speak to the study team for any reason, please call Avril Mansfield at 416-597-3422 extension 7831. **If you have any questions about your rights as a research participant or have concerns about this study, call the Chair of the University Health Network Research Ethics Board (UHN REB) or the Research Ethics office number at 416-581-7849.** The REB is a group of people who oversee the ethical conduct of research studies. The UHN REB is not part of the study team. Everything that you discuss will be kept confidential.

You will be given a signed copy of this consent form.

Consent

This study has been explained to me and any questions I had have been answered.

I know that I may leave the study at any time. I agree to the use of my information as described in this form. I agree to take part in this study.

 Signature Date

My signature means that I have explained the study to the participant named above. I have answered all questions.

 Name of person obtaining consent Signature Date

Was the participant assisted during the consent process? YES NO

If **YES**, please check the relevant box and complete the signature space below:

The person signing below acted as an interpreter for the participant during the consent process and attests that the study as set out in this form was accurately interpreted has had any questions answered.

 Name of interpreter Signature Date

 Relationship to participant Language

The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to, and has had any questions answered.

 Name of witness Signature Date

 Relationship to participant



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Page no.
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	2-4
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	1
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	1
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	7
	6b	Explanation for choice of comparators	10
Objectives	7	Specific objectives or hypotheses	8

1				
2	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	8
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8	Methods:			
9	Participants,			
10	interventions			
11	, and			
12	outcomes			
13				
14	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8-9
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20	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
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24	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10
25				
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29		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	9-10
30				
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33				
34		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	9-10
35				
36				
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39		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a
40				
41				
42	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-12
43				
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51	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1 Table 1
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2	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
3				
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6				
7	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	12-13
8				
9				

Methods: Assignment of interventions (for controlled trials)

Allocation:

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16				
17	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	13
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26	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	13
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33	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
34				
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37	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
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41		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
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Methods: Data collection, management, and analysis

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51	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13
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2		18b	Plans to promote participant retention and complete follow-	13
3			up, including list of any outcome data to be collected for	
4			participants who discontinue or deviate from intervention	
5			protocols	
6				
7	Data	19	Plans for data entry, coding, security, and storage, including	14
8	management		any related processes to promote data quality (eg, double	
9			data entry; range checks for data values). Reference to	
10			where details of data management procedures can be	
11			found, if not in the protocol	
12				
13				
14	Statistical	20a	Statistical methods for analysing primary and secondary	14-15
15	methods		outcomes. Reference to where other details of the statistical	
16			analysis plan can be found, if not in the protocol	
17				
18		20b	Methods for any additional analyses (eg, subgroup and	n/a
19			adjusted analyses)	
20				
21				
22		20c	Definition of analysis population relating to protocol non-	n/a
23			adherence (eg, as randomised analysis), and any statistical	
24			methods to handle missing data (eg, multiple imputation)	
25				
26	Methods:			
27	Monitoring			
28				
29	Data	21a	Composition of data monitoring committee (DMC); summary	15
30	monitoring		of its role and reporting structure; statement of whether it is	
31			independent from the sponsor and competing interests; and	
32			reference to where further details about its charter can be	
33			found, if not in the protocol. Alternatively, an explanation of	
34			why a DMC is not needed	
35				
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38		21b	Description of any interim analyses and stopping guidelines,	n/a
39			including who will have access to these interim results and	
40			make the final decision to terminate the trial	
41				
42	Harms	22	Plans for collecting, assessing, reporting, and managing	16-17
43			solicited and spontaneously reported adverse events and	
44			other unintended effects of trial interventions or trial conduct	
45				
46				
47	Auditing	23	Frequency and procedures for auditing trial conduct, if any,	n/a
48			and whether the process will be independent from	
49			investigators and the sponsor	
50				
51				
52	Ethics and			
53	dissemination			
54				
55	Research	24	Plans for seeking research ethics committee/institutional	17
56	ethics		review board (REC/IRB) approval	
57	approval			
58				
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1				
2	Protocol	25	Plans for communicating important protocol modifications	17
3	amendments		(eg, changes to eligibility criteria, outcomes, analyses) to	
4			relevant parties (eg, investigators, REC/IRBs, trial	
5			participants, trial registries, journals, regulators)	
6				
7	Consent or	26a	Who will obtain informed consent or assent from potential	17-18
8	assent		trial participants or authorised surrogates, and how (see	
9			Item 32)	
10				
11				
12		26b	Additional consent provisions for collection and use of	n/a
13			participant data and biological specimens in ancillary	
14			studies, if applicable	
15				
16	Confidentiality	27	How personal information about potential and enrolled	18
17			participants will be collected, shared, and maintained in	
18			order to protect confidentiality before, during, and after the	
19			trial	
20				
21				
22	Declaration of	28	Financial and other competing interests for principal	18
23	interests		investigators for the overall trial and each study site	
24				
25	Access to	29	Statement of who will have access to the final trial dataset,	18
26	data		and disclosure of contractual agreements that limit such	
27			access for investigators	
28				
29				
30	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for	19
31	post-trial care		compensation to those who suffer harm from trial	
32			participation	
33				
34	Dissemination	31a	Plans for investigators and sponsor to communicate trial	19
35	policy		results to participants, healthcare professionals, the public,	
36			and other relevant groups (eg, via publication, reporting in	
37			results databases, or other data sharing arrangements),	
38			including any publication restrictions	
39				
40				
41		31b	Authorship eligibility guidelines and any intended use of	19
42			professional writers	
43				
44		31c	Plans, if any, for granting public access to the full protocol,	18
45			participant-level dataset, and statistical code	
46				
47				
48	Appendices			
49				
50	Informed	32	Model consent form and other related documentation given	Appendix
51	consent		to participants and authorised surrogates	
52	materials			
53				
54	Biological	33	Plans for collection, laboratory evaluation, and storage of	n/a
55	specimens		biological specimens for genetic or molecular analysis in the	
56			current trial and for future use in ancillary studies, if	
57			applicable	
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1 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013
2 Explanation & Elaboration for important clarification on the items. Amendments to the
3 protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT
4 Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)"
5 license.
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Determining the optimal dose of reactive balance training after stroke – study protocol for a pilot randomized controlled trial

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1. ADMINISTRATIVE INFORMATION

Title: Determining the optimal dose of reactive balance training after stroke – study protocol for a pilot randomized controlled trial

Authors: Avril Mansfield,¹⁻³ Elizabeth L. Inness,^{1,2} Cynthia J Danells,^{1,2} David Jagroop,¹ Tanvi Bhatt,⁴ Andrew H Huntley¹

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Key words: Stroke; Physiotherapy; Postural balance; Accidental falls; Pilot projects

Word count: 4,452

Protocol version date: 15 November 2019; Original

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Contributorship: AM conceived of the study, is the grant holder, and drafted the manuscript. AM, ELI, and CJD developed the intervention. AM, ELI, CJD, DJ, TB and AHH contributed to study design, writing/editing the manuscript, and approved the final manuscript.

1
2 26 **2. WHO DATASET**

3
4 27 **1. Trial registration:** clinicaltrials.gov, NCT04219696

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6 28 **2. Date of registration:** 7 January 2020

7
8 29 **3. Secondary identification numbers:** Not applicable

9
10 30 **4. Sources of monetary or material support:** This study is supported by the Heart and Stroke
11 31 Foundation Canadian Partnership for Stroke Recovery. AM holds a New Investigator Award
12 32 from the Canadian Institutes of Health Research (MSH-141983). We also acknowledge the
13 33 support of the Toronto Rehabilitation Institute; equipment and space have been funded with
14 34 grants from the Canada Foundation for Innovation, Ontario Innovation Trust, and the Ministry
15 35 of Research and Innovation. These funding sources had no role in the design of this study and
16 36 will not have any role during its execution, analysis, interpretation of the data, or decision to
17 37 submit results.

18 38 **5. Primary sponsor:** Avril Mansfield

19 39 **6. Secondary sponsors:** Elizabeth Inness, Tanvi Bhatt

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21 41 2A2; tel: 416-597-3422 ext 7831; e-mail: avril.mansfield@uhn.ca

22 42 **8. Contact for scientific queries:** Avril Mansfield; address: 550 University Ave, Toronto, ON,
23 43 M5G 2A2; tel: 416-597-3422 ext 7831; e-mail: avril.mansfield@uhn.ca

24 44 **9. Public title:** Determining the optimal dose of reactive balance training after stroke

25 45 **10. Scientific title:** Determining the optimal dose of reactive balance training after stroke – a pilot
26 46 study

27 47 **11. Countries of recruitment:** Canada

28 48 **12. Interventions:** Reactive balance training. A research physiotherapist will oversee reactive
29 49 balance training (RBT) in collaboration with participants' regular physiotherapists to ensure
30 50 consistent RBT delivery across participants. Training strategies will be individualized to each

1
2 51 participant, based on their balance impairments and rehabilitation goals. The RBT program
3
4 52 includes multi-directional 'internal' and 'external' balance perturbations. Internal perturbations
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6 53 are achieved by asking the participant to complete tasks that challenge balance control, such
7
8
9 54 that they lose balance when attempting to perform the task (e.g., kicking a soccer ball). External
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11 55 perturbations are delivered manually using a push or pull from the physiotherapist. As
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13 56 participants improve their reactive balance control, difficulty will be increased by shifting task
14
15 57 requirements along a continuum from stable to mobile, and from predictable to unpredictable,
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17
18 58 and by increasing perturbation magnitude or imposing sensory or environmental challenges.
19

20 59 **13. Key inclusion and exclusion criteria:** Inclusion criteria: sub-acute stroke; receiving out-patient
21
22 60 rehabilitation at the Toronto Rehabilitation Institute; can stand independently for >30 seconds;
23
24
25 61 can walk with or without a gait aid (but without assistance of another person) for >10 metres;
26
27 62 and living in the community. Exclusion criteria: completed reactive balance training during in-
28
29 63 patient rehabilitation; lower-extremity amputation, weight-bearing restrictions, recent lower-
30
31 64 extremity injury or surgery (e.g., fracture), acute back or lower-limb pain, halo, aspen collar,
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34 65 history of fragility fracture and/or severe osteoporosis/osteopenia, contractures that prevent
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36 66 neutral hip or ankle; activity restrictions following cardiac event/surgery, abnormal or unstable
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39 67 cardiovascular responses to exercise, arterial dissection; severe spasticity in the legs; cognitive
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41 68 impairment (i.e., unable to understand the purpose of training and/or to provide informed
42
43 69 consent); and/or acute illness (e.g., vomiting, fever), weight > 150 kg (exceeds safety harness
44
45 70 weight limits), colostomy bags, indwelling catheter, infection, pressure sore on pelvis or trunk.
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48 71 **14. Study type:** Pilot parallel randomized controlled trial.
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50 72 **15. Date of first enrolment:** June 2020 (anticipated).
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52 73 **16. Target sample size:** 36
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55 74 **17. Recruitment status:** Pending.
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18. Primary outcome: Rate of falls in daily life for six months post-discharge from out-patient rehabilitation.

19. Secondary outcomes: Rate of accrual, rate of missing data, intervention fidelity.

For peer review only

3. ABSTRACT

Introduction: Falls risk post-stroke is highest soon after discharge from rehabilitation. Reactive balance training (RBT) aims to improve control of reactions to prevent falling after a loss of balance. In healthy older adults, a single RBT session can lead to lasting improvements in reactive balance control and prevent falls in daily life. While increasing the dose of RBT does not appear to lead to additional benefit for healthy older adults, stroke survivors, who have more severely impaired balance control, may benefit from a higher RBT dose. Our long-term goal is to determine the optimal dose of RBT in people with sub-acute stroke. This assessor-blinded pilot randomized controlled trial aims to inform the design of a larger trial to address this long-term goal.

Methods and analysis: Participants (n=36) will be attending out-patient stroke rehabilitation, and will be randomly allocated to one of three groups: 1, 3, or 6 RBT sessions. RBT will replace a portion of participants' regular physiotherapy so that the total physical rehabilitation time will be the same for the 3 groups. Balance and balance confidence will be assessed at: 1) study enrolment; 2) out-patient rehabilitation discharge; and 3) 6 months post-discharge. Participants will report falls and physical activity for 6 months post-discharge. Pilot data will be used to plan the larger trial (i.e., sample size estimate using fall rates, and which groups should be included based on between-group trends in pre-to-post training effect sizes for reactive balance control measures). Pilot data will also be used to assess the feasibility of the larger trial (i.e., based on the accrual rate, outcome completion rate, and feasibility of prescribing specific training doses).

Ethics and dissemination: Institutional research ethics approval has been received. Study participants will receive a lay summary of results. We will also publish our findings in a peer-reviewed journal.

4. STRENGTHS AND LIMITATIONS

- The intervention will replace a portion of participants routine physiotherapy during out-patient rehabilitation. Therefore, the findings will be directly relevant to clinical practice.
- Conversely, there is a risk that patients will decline participation in the study, which requires consent to being randomized to a specific dose of reactive balance training, as they will not want their rehabilitation care to be disrupted.
- This is a pilot study, so it is unlikely that we will be able to make definitive decisions regarding the optimal dose of reactive balance training post-stroke.

5. INTRODUCTION

5.1 Background and rationale

Falls are the most prevalent complications during all stages of stroke recovery.¹ Along with physical injuries, 88% of people with stroke who fall develop fear of falling.² Falls and fear of falling can lead to inactivity, deconditioning, and lower functional capacity, further increasing fall risk^{3,4} and reducing quality of life.⁵

Conventional balance training, where the goal is to maintain balance during the balance-challenging exercises, reduces falls in older adults,⁶ but not after stroke.^{7,8} Reactive balance training (RBT), where clients experience repeated postural perturbations (or loss of balance),^{9,10} is a novel type of exercise that aims to improve reactive balance control. RBT can prevent falls in older adults and people with Parkinson's disease.¹¹ Our non-randomized study suggests that RBT reduces fall rates after discharge from stroke rehabilitation.¹² In our previous study, the intervention was implemented as part of routine care, and the dose of RBT depended on client goals and preferences and length of stay, rather than being prescribed by the study protocol. Participants completed 1-12, 30-minute RBT sessions (median of 6 sessions).¹²

Unlike other forms of exercise (e.g., resistance training or aerobic exercise), where improvements in physical fitness take weeks or months of regular training,¹³ improved reactive balance control with RBT seems to occur with few repetitions, and is maintained for several months without training. Among healthy older adults, just 24 perturbations within a single session of RBT is sufficient to lead to lasting improvements (i.e., 6-12 months) in reactive balance control,¹⁴ and prevent falls in daily life.¹⁵ One study in people with chronic stroke found that improved reactive balance control with a single session of RBT was retained for 3 weeks post-training.¹⁶ Almost doubling the dose of RBT does not appear to lead to additional benefit for healthy older adults;¹⁷ however, it is possible that those with stroke would benefit from additional RBT as they have more severely impaired balance than healthy older adults.¹⁸ While additional training may also promote sustained improvements in reactive

1
2 136 balance control beyond 3 weeks,¹⁹⁻²¹ in one study that included people with sub-acute stroke reduced
3
4 137 fall rates up to six months post-training were reported when 29% of participants completed only one
5
6 138 30-minute session of RBT.¹² The sub-acute phase is a crucial period for reactive balance training, due
7
8
9 139 to the high potential for neuroplasticity in this early phase of recovery,²² and to the high risk of falls
10
11 140 early after stroke.²³ Therefore, there is a need to establish optimal RBT training parameters in the sub-
12
13 141 acute stroke population.

18 143 **5.2 Objectives and research questions**

19
20 144 The long-term goal of this work is *to determine the optimal dose of RBT in people with sub-acute*
21
22 *stroke*. This assessor-blinded pilot randomized controlled trial (RCT) aims *to inform the design of a*
23 145 *larger trial to address this long-term goal*. Specifically, the following questions about the larger trial
24
25 146 will be answered with this pilot study:
26

- 27 147
28
29 148 1) what is the optimal sample size;
- 30
31
32 149 2) how long will it take to achieve this sample size;
- 33
34 150 3) are the proposed secondary outcome measures feasible;
- 35
36 151 4) how feasible is it to prescribe a specific dose of RBT to people with sub-acute stroke within
37
38 routine out-patient rehabilitation; and
- 39 152
40
41 153 5) what two intervention groups should be included in the larger trial?
- 42

43 154 44 45 155 **5.3 Trial design**

46
47
48 156 The current paper describes the protocol for an assessor-blinded pilot RCT (Figure 1), following the
49
50 157 SPIRIT guidelines and checklist.²⁴ People who are attending out-patient stroke rehabilitation will be
51
52 158 randomly assigned to one of three different doses of reactive balance training (RBT). Reactive balance
53
54 control, functional balance, and balance confidence will be measured at study enrolment (within days
55 159 of admission to out-patient rehabilitation), discharge from out-patient rehabilitation, and 6 months post-
56
57 160

1
2 161 discharge. Falls in daily life, physical activity, and participation will be assessed for 6 months post-
3
4 162 discharge.

5 6 163 7 8 9 164 *5.3.1 Patient and public involvement*

10
11 165 This study was designed without patient involvement. Patients were not invited to comment on the
12
13 166 study design and were not consulted to develop patient relevant outcomes. Some trial design elements
14
15
16 167 were informed by participant feedback from our previous RBT study.¹⁹ Patients were not invited to
17
18 168 contribute to the writing or editing of this document for readability or accuracy.
19

20 169 21 22 23 170 **6. METHODS: PARTICIPANTS, INTERVENTIONS, AND OUTCOMES**

24 25 171 **6.1 Study setting**

26
27 172 This study will take place at the Toronto Rehabilitation Institute, University Health Network. This
28
29 173 facility provides specialized in- and out-patient stroke rehabilitation to individuals in the sub-acute
30
31
32 174 stage of stroke recovery. Out-patient stroke rehabilitation at the Toronto Rehabilitation Institute
33
34 175 typically includes 45 minutes of physiotherapy 2-5 times/week for at least 4 weeks, with most patients
35
36 176 receiving 8 weeks of out-patient rehabilitation.
37
38

39 177 40 41 178 **6.2 Participants**

42
43 179 Participants will be people with sub-acute stroke (<6-months post-stroke) who are receiving out-patient
44
45 180 rehabilitation at the Toronto Rehabilitation Institute. Participants will be eligible if they can: 1) stand
46
47
48 181 independently for >30s; 2) walk with or without a gait aid (but without assistance of another person)
49
50 182 for >10m; and 3) are living in the community. Participants will be excluded if they have:

- 51
52
53 183 • Completed RBT during in-patient rehabilitation;

- 184 • Lower extremity amputation, weight-bearing restrictions, recent lower-extremity injury or
185 surgery (e.g., fracture), acute back or lower-limb pain, halo, aspen collar, history of fragility
186 fracture and/or severe osteoporosis/osteopenia, contractures that prevent neutral hip or ankle;
- 187 • Activity restrictions following cardiac event/surgery, abnormal or unstable cardiovascular
188 responses to exercise, arterial dissection;
- 189 • Severe spasticity in the legs that prevents the individual from safely accepting weight on the
190 limb;
- 191 • Cognitive impairment (i.e., unable to understand the purpose of training and/or to provide
192 informed consent), as determined by the healthcare team; and/or
- 193 • Acute illness (e.g., vomiting, fever), extreme obesity (exceeds safety harness system weight
194 limits), colostomy bags, indwelling catheter, infection, pressure sore on pelvis or trunk.

195 After participants provide consent, eligibility will be confirmed using information in the participants'
196 hospital chart, by consulting members of the patient's healthcare team, and by consulting the
197 participant themselves. Participants will still receive their usual care, while participating in the study.

198 Participants will be informed that they are free to withdraw from the study at any time point,
199 without consequence. If participants ask to be withdrawn from the study, any data collected from them
200 up to that point will be used to answer the research questions. Participants may also be withdrawn from
201 the study due to changes in their health status that affect eligibility.

203 **6.3 Interventions**

204 Participants will be allocated to one of three groups: one, three, or six, 45-minute RBT sessions. RBT
205 will replace a portion of participants' regular physiotherapy, so that the total amount of physical
206 rehabilitation will not be affected by study participation, and will be approximately equal for the three
207 groups. Each 45-minute session will be entirely dedicated to RBT, and will include up to 60

1
2 208 perturbations. The proposed session duration and number of perturbations per session is double that of
3
4 209 our previous sub-acute study, whereas the number of sessions is halved.¹² This previous study was
5
6 210 conducted during in-patient rehabilitation, where patients are typically provided with 60-minutes of
7
8
9 211 physiotherapy 5 days per week. Within this schedule, patients could easily complete 30 minutes of
10
11 212 RBT, leaving 30 minutes per day for other physical therapies. However, as out-patient physiotherapy is
12
13 213 only 45 minutes per session, the proposed dosages more easily fit into most out-patient rehabilitation
14
15 214 therapy schedules. From our team's previous research^{12,19} and experience with clinical implementation
16
17
18 215 of RBT in stroke rehabilitation, we expect that participants will be able to tolerate the 45-minute
19
20 216 sessions of RBT. Rest breaks will be scheduled into each session, and will be provided when requested
21
22
23 217 by participants.

24
25 218 A research physiotherapist will oversee RBT in collaboration with participants' regular
26
27 219 physiotherapists to ensure consistent RBT delivery across participants. Training strategies will be
28
29 220 individualized to each participant, based on their balance impairments and rehabilitation goals.^{12,19} For
30
31 221 example, if a participant has low foot clearance when executing reactive steps, then obstacles will be
32
33 222 placed on the floor and the participant will be encouraged to step over the obstacles during voluntary
34
35 223 and reactive stepping. If a participant has a goal to return to a specific activity then aspects of that
36
37 224 activity will be included in the training sessions (e.g., if returning to golfing is a goal, the participant
38
39 225 may train on a compliant surface to simulate uneven outdoor terrain). Further details of the specific
40
41 226 balance training approaches that will be used and how training will be tailored to individual
42
43 227 participants can be found in our previous paper.¹⁹ The RBT program includes multi-directional
44
45 228 'internal' and 'external' balance perturbations. Internal perturbations are achieved by asking the
46
47 229 participant to complete tasks that challenge balance control, such that they lose balance when
48
49 230 attempting to perform the task (e.g., kicking a soccer ball). External perturbations are delivered
50
51 231 manually using a push or pull from the physiotherapist while the participant is either standing still or
52
53 232 doing a voluntary task, like marching on the spot; when the physiotherapist is positioned behind the
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1
2 233 participant, the direction and timing of the push or pull can be unpredictable to the participant. As
3
4 234 participants improve their reactive balance control, difficulty will be increased by shifting task
5
6 235 requirements along a continuum from stable to mobile, and from predictable to unpredictable, and by
7
8
9 236 increasing perturbation magnitude (i.e., by increasing the force of the push/pull) or imposing sensory or
10
11 237 environmental challenges.²⁵
12

13 238 14 15 16 239 **6.4 Outcome measures**

17
18 240 To assess feasibility of the study, we will document rates of accrual (i.e., number of patients
19
20 241 approached to participate in the study versus the number who provide consent), number of training
21
22 242 sessions attended/missed, reasons for missed sessions, rate of missing data for the outcomes described
23
24
25 243 below, and rate of withdrawal from the study.
26

27 244 Table 1 summarizes additional outcome measures. Demographic, stroke information, and
28
29 245 medical history will be extracted from participants' hospital charts. Participants will complete a
30
31
32 246 questionnaire at baseline that asks about their social supports, employment, familial responsibilities,
33
34 247 living situation etc., which are factors that could influence fall risk. Many of these questions have been
35
36 248 adapted from the Canadian Longitudinal Study on Aging.²⁶ The National Institutes of Health Stroke
37
38
39 249 Scale (NIH-SS)²⁷ will be scored at study enrolment. Clinical assessments will be scored by a blinded
40
41 250 research assistant at three time points: 1) study enrolment (as soon as possible after admission to out-
42
43 251 patient rehabilitation); 2) discharge from out-patient rehabilitation; and 3) 6 months post-discharge.
44
45
46 252 Tests will include: Chedoke-McMaster Stroke Assessment (CMSA)²⁸ foot and leg scores; mini-
47
48 253 Balance Evaluation Systems Test (mini-BEST);²⁹ Activities-specific Balance Confidence (ABC)
49
50 254 scale;³⁰ and reactive balance control following unpredictable and novel perturbations.
51

52
53 255 To assess reactive balance control, participants will be outfitted with reflective markers, and
54
55 256 will complete 8-10 walking trials on a movable platform. There will be four force plates embedded in
56
57 257 the movable platform. On two trials, the platform will move forward suddenly on heel strike (i.e., when
58
59

1
2 258 one of the force plates is loaded) to trigger a slip-like perturbation.³¹ On two other trials, the platform
3
4 259 will move backward suddenly on toe-off (i.e., when one of the force plates is unloaded) to trigger a
5
6 260 trip-like perturbation. Each slip or trip trial will be triggered on heel-strike or toe-off, respectively, of
7
8
9 261 each of the left and right limbs. The perturbation waveform will consist of a 300 ms square-wave
10
11 262 acceleration, followed immediately by 300 ms deceleration (peak acceleration up to 1.5m/s²).³¹ The
12
13 263 platform will only move during these four trials; the remaining 4-6 trials will consist of unperturbed
14
15
16 264 walking. The slip/trip and unperturbed walking trials will be presented in a pseudo-random order to
17
18 265 ensure that participants cannot predict the timing, direction, or perturbed limb for these trials. This
19
20 266 unpredictability will help ensure that any changes are not simply due to practice effects on the specific
21
22 267 task. While there may be some improvement in responses to the perturbation simply due to repetition
23
24
25 268 of the task (i.e., not due to training effects), previous work suggests that experiencing a single slip or
26
27 269 trip perturbation does not lead to large and lasting improvements responses to the perturbations.^{32,33}
28
29
30 270 These perturbations differ from what will be used during training, and will measure transfer of training
31
32 271 to a novel and ecological loss of balance. Three-dimensional motion capture will record the locations of
33
34 272 the reflective markers in space. Biomechanical stability when responding to the perturbation will be
35
36 273 measured using an established method that considers the distance between the centre of mass and base
37
38
39 274 of support;^{31,34} in general, a more posteriorly- (slip) or anteriorly-located (trip) centre of mass in
40
41 275 relation to the perturbed lower limb is considered less stable.
42

43 276 Participants will be asked to report falls (“an event that results in a person coming to rest
44
45 277 unintentionally on the ground or other lower level”³⁵) in the 6 months post-discharge. Participants will
46
47
48 278 be provided with stamped, addressed postcards to mail to the research team every 2 weeks for 6 months
49
50 279 post-discharge. Postcards will contain a calendar, on which participants will record falls. The blinded
51
52 280 research assistant will call participants who do not return the postcard to determine if any falls
53
54
55 281 occurred. The research assistant will contact participants reporting a fall to complete a short
56
57
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questionnaire determining the cause and consequences of the fall. This method is considered the ‘gold standard’ for fall reporting.³⁶

Participants will also report physical activities using the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD),³⁷ and participation in daily life using the Subjective Index of Physical and Social Outcome (SIPSO) at 2-, 4- and 6-months post-discharge.

6.5 Sample size

We will aim to recruit 12 participants per group (36 participants total), as recommended for pilot studies.³⁸

6.6 Recruitment

Participants will be recruited from the Toronto Rehabilitation Institute University Centre out-patient stroke rehabilitation program. This program admits approximately 200 individuals with stroke per year.

Potentially eligible participants will be identified by the patients’ primary treating physiotherapist.

Participants will be reimbursed for any travel expenses (e.g., public transit, taxi, or parking) they incur to attend data collection appointments; participants will not be reimbursed for travel expenses for the intervention as they will occur as part of routine care. Participants will also receive a \$50 gift card upon completion of the study as a modest incentive to participate.

7. METHODS: ASSIGNMENT OF INTERVENTIONS

7.1 Group allocation

Participants will be assigned using blocked randomization to one of the three different doses of RBT (block size: 6). The random allocation sequence will be computer generated. Blocked randomization will ensure equal numbers allocated to each group. Group allocation will be performed centrally by the

1
2 306 principal investigator, who will not be involved in recruiting, scoring assessments, or administering the
3
4 307 interventions (i.e., concealed allocation).
5

6 308 7 8 9 309 **7.2 Blinding**

10
11 310 Outcome measures will be obtained by a research assistant who will be blinded to group allocation. At
12
13 311 the discharge and follow-up study visits, the research assistant will be asked to guess the participants'
14
15
16 312 group allocation, and if the research assistant received any information about participant group
17
18 313 allocation that led to unblinding. Participants cannot be blinded to group allocation. Data analysis will
19
20 314 be conducted by an individual who is not blinded to group allocation.
21
22
23 315

24 25 316 **8. METHODS: DATA COLLECTION, MANAGEMENT, AND ANALYSIS**

26 27 317 **8.1 Data collection methods**

28
29 318 Data will be collected primarily by the research assistant either directly from the participant or by chart
30
31
32 319 review (see Table 1 for further details). The research assistant has received training regarding data
33
34 320 collection from the principal investigator. Questionnaires will be completed via in person interview at
35
36 321 enrolment, and over the telephone at the follow-up time points.
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38
39 322

40 41 323 **8.2 Data management**

42
43 324 Electronic data will be stored on secure institutional servers. Hard copies of files containing de-
44
45 325 identified data will be stored in locked cabinets and/or in offices that are locked when not occupied.
46
47
48 326

49 50 327 **8.3 Data analysis**

51
52 328 Data analysis will address the research questions as described below.
53

- 54 329 1. *What is the optimal sample size?* The proposed primary outcome in the larger trial will be rate of
55
56
57 330 falls in daily life. The one-session group is expected to show minimal improvements in reactive
58
59
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- 1
2 331 balance control and fall risk. Therefore, the rate of falls (number of falls per person-year) in the
3
4 332 one-session group, reported over the 6-months post-discharge, and a clinically meaningful 30%
5
6 333 reduction in fall rates, will be used to estimate sample size for the larger trial.³⁹
7
8
9 334 2. *How long will it take to achieve this sample size?* We will use the accrual rate (number of
10
11 335 participants recruited per month) and proportion of participants who withdraw from the study to
12
13 336 estimate how long it will take to achieve the target sample size in the larger trial.
14
15
16 337 3. *Are the proposed secondary outcome measures feasible?* Our previous work supports feasibility of
17
18 338 data collection using most of the measures in this population.¹² However, we have not previously
19
20 339 tested the slip- and trip-like perturbations in this population. We will report between-group effect
21
22 340 sizes and completeness of data collection for responses to the slip- and trip-like perturbations, and
23
24 341 other outcome measures (i.e., Chedoke-McMaster Stroke Assessment, Mini-Balance Evaluation
25
26 342 Systems Test, Activities-specific Balance Confidence Scale, Physical Activity Scale for
27
28 343 Individuals with Physical Disabilities, and Subjective Index of Physical and Social Outcome); the
29
30 344 larger trial will only include outcomes with $\geq 80\%$ completion rate.
31
32
33
34 345 4. *How feasible is it to prescribe specific dose of RBT to people with sub-acute stroke?* The feasibility
35
36 346 of prescribing a specific RBT dose during patients' routine rehabilitation is not known. Participants
37
38 347 assigned to the 3- or 6-session groups or their physiotherapists may decline sessions if they feel
39
40 348 they is not beneficial to their care. Likewise, participants assigned to the 1- or 3-session groups or
41
42 349 their physiotherapists may feel that they can benefit from additional RBT sessions. The dose will
43
44 350 be considered feasible if the mean number of sessions and number of perturbations per session is
45
46 351 75-100% of prescribed.
47
48
49
50 352 5. *What two intervention groups should be included in the larger trial?* The larger trial will compare
51
52 353 one session of RBT with a higher dose. We will use the reactive control sub-scale of the mini-
53
54 354 BEST as a measure of effect of RBT on reactive balance control in each group. Scores on this sub-
55
56 355 scale have been shown to improve with a high dose of RBT in people with chronic stroke.¹⁹ We
57
58
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60

1
2 356 will calculate the pre-to-post training effect sizes for this sub-scale for each group (i.e., mean
3
4 357 difference in the score from admission to discharge). The minimum detectable change for the total
5
6 358 mini-BEST score in people with stroke is 3 points⁴⁰ (i.e., ~10% of the maximum score). The
7
8
9 359 minimum detectable change for individual sub-scales have not been established, but we will
10
11 360 assume that this is 10% of the maximum score for the subscale (i.e., 0.6 points). Therefore, if the
12
13 361 pre-to-post training effect sizes are within 0.6 points for the three-session and six-session groups,
14
15
16 362 then the larger trial will include the one-session and three-session groups. However, if effect sizes
17
18 363 reveal a trend towards greater improvement for the six-session group, then the larger trial will
19
20 364 include the one-session and six-session groups.

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22
23 365
24
25 366 Data will be analyzed at the end of the study. Therefore, there is no plan for interim analyses of
26
27 367 primary and/or secondary variables.
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29
30 368

31 369 **9. METHODS: MONITORING**

32 370 **9.1 Data monitoring**

33
34 371 There is no data monitoring committee for this study; several previous studies have already
35
36
37 372 demonstrated that reactive balance training is safe for people with stroke, with few adverse events
38
39 373 reported.^{12,16,19,20} Adverse events that meet all three of the following criteria will be reported
40
41 374 immediately to the institution's Research Ethics Board, as is routine practice: 1) unexpected in terms of
42
43 375 nature, severity, or frequency; 2) related or possibly related to participation in the research; and 3)
44
45
46 376 suggests a potential increased in risk of harm to research participants or others. All adverse events will
47
48 377 be collated and evaluated bi-annually by the principal investigator.
49
50 378

51 379 **9.2 Potential harms**

1
2 380 In a previous study, mild adverse events related to RBT in people with stroke were delayed-onset
3
4 381 muscle soreness, fatigue, or exacerbation of joint pain (11%, 7%, and 32% of participants,
5
6 382 respectively),¹⁹ which did not require medical attention, but resulted in reduced intervention intensity
7
8
9 383 until they resolved (typically by the following session). Of note, the frequency and severity of adverse
10
11 384 events are similar for the RBT group and control group, who completed more ‘traditional’ balance
12
13 385 training.¹⁹ Therefore, these types of adverse events are typical of similar exercise programs, and not
14
15
16 386 specific to RBT.

17
18 387 As the assessment and intervention includes tasks that are deliberately challenging to balance
19
20 388 control, there is a small risk that participants, upon loss of balance, will fall. Appropriate precautions
21
22 389 will be taken to ensure patient safety during these tasks. Interventions will be administered by a trained
23
24
25 390 and licensed physiotherapist who will tailor the training to the patient’s abilities. Assessments will be
26
27 391 completed by a trained research assistant with a health sciences background. A safety harness attached
28
29 392 to a secure point overhead will be worn for all postural perturbations to prevent a fall to the floor if the
30
31
32 393 individual fails to regain stability. Additionally, the research assistant or physiotherapist can provide
33
34 394 assistance to prevent a fall. We have administered tens of thousands of postural perturbations to over
35
36 395 500 individuals with varying balance abilities in previous research studies and clinical activities and no
37
38
39 396 participant suffered an injury as a result of an induced postural perturbation. However, even if the
40
41 397 participant is caught by the safety harness or researcher, there is a very small chance that participants
42
43 398 will suffer a physical injury (e.g., sprain or bruise). In the event of a minor physical injury, the
44
45
46 399 physiotherapist will provide first aid, will advise the participant regarding follow-up with a medical
47
48 400 professional (e.g., family doctor) and home treatment (e.g., rest, ice, compression, elevation), and will
49
50 401 follow-up with the participant after a day or two.

51
52 402 The physiotherapist will communicate regularly with the participant’s care team about changes
53
54
55 403 in health status that could affect risk profile. Participants will be withdrawn if their health changes such
56
57 404 that they would no longer be eligible for the study (i.e., one of the exclusion criteria applies to them).
58

10. ETHICS AND DISSEMINATION

10.1 Research ethics approval

Research ethics approval has been received by the Research Ethics Board of the University Health Network (Study ID: 19-6001, approved 17 January 2020).

10.2 Protocol amendments

Substantive changes to the design or conduct of the study will require a formal amendment to the study protocol. Such substantive amendments will be agreed upon by the study investigators and will be approved by the Research Ethics Board of the University Health Network prior to implementation.

Minor administrative changes to study documents (e.g., correcting a typographical error or clarifying a questionnaire item) may also be implemented, with the Research Ethics Board notified of the changes.

10.3 Consent

Potentially eligible participants will be identified by the patients' primary treating physiotherapist. The physiotherapist will ask patients if they are interested in speaking with a research assistant regarding the study. If patients agree, they will be approached by a member of the research team (DJ, CJD or a delegate acting on their behalf) who will explain the study and provide patients with the study information sheet and consent form (Appendix). Research personnel will answer the patient's questions about the study. Patients may discuss the study with their friends, family members, or healthcare providers. Patients may take as long as necessary to decide if they wish to participate in the study; however, if a patient has not decided before they are discharged then we will assume they have declined participation. The informed consent process will be documented by research personnel.

10.4 Confidentiality

1
2 430 Personal information is any information that could identify participants. If participants agree to join this
3
4 431 study, the following personal information will only be accessible to the research team, for contact
5
6 432 purposes: name, telephone number, mailing address, and e-mail address (if provided). A number of
7
8
9 433 steps will be taken to ensure protection of personal health information. All information collected during
10
11 434 this study, including the participant's personal information, will be kept confidential and will not be
12
13 435 shared with anyone outside the study unless required by law. Electronic data will be stored on secure
14
15
16 436 servers for 10 years. After 10 years the data will be deleted from the servers. Electronic files containing
17
18 437 patient names and contact information will be password protected, and will be stored separately from
19
20 438 study data. Hard copies of files containing de-identified data will be stored in locked cabinets and/or in
21
22
23 439 offices that are locked when not occupied. Consent forms will be stored in locked cabinets/offices
24
25 440 separately from other data. Only those individuals who require access to the data for the purpose of this
26
27 441 study will be provided with the password to the file containing identifiers and/or the keys to the locked
28
29
30 442 cabinet/office.

34 444 **10.5 Declaration of interests**

35
36 445 The authors declare that they have no competing interests related to this study.
37
38
39 446

41 447 **10.6 Access to data**

42
43 448 The principal investigator (AM) will have access to the full dataset. There is no current plan to make
44
45
46 449 the participant-level dataset available publicly; however, the dataset may be made available in future
47
48 450 via a Data Access Committee, if such a committee is established by the institution.
49
50 451

52 452 **10.7 Ancillary and post-trial care**

53
54
55 453 The University Health Network will be responsible for providing out-of-pocket expenses to ensure that
56
57 454 a participant receives immediate medical care in the event that the participant experiences an adverse
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1
2 455 health event (e.g., injury) as a result of participation in the study. Patients do not typically receive
3
4 456 follow-up after discharge from rehabilitation; therefore, there is no plan for any post-trial care.
5

6 457 7 8 9 458 **10.8 Dissemination policy**

10
11 459 Participants will receive a letter of appreciation at the end of the study, which may include a brief
12
13 460 summary of the study results. Study results will be shared with the academic community via
14
15
16 461 publication in peer-reviewed journals and presentations at conferences. We will aim to submit a paper
17
18 462 describing analysis of the primary and secondary outcomes within 6 months of completing data
19
20 463 collection. All individuals who meet the International Committee of Medical Journal Editors criteria for
21
22 464 authorship will be included as authors on any publications arising from this work. We will share results
23
24
25 465 directly with physiotherapists through interactive workshops (e.g., at the Canadian Physiotherapy
26
27 466 Association meeting). We are developing a toolkit to assist physiotherapists implementing RBT. The
28
29
30 467 results of the larger trial will be incorporated into the toolkit as recommendations for RBT dose in sub-
31
32 468 acute stroke.
33

34 469 35 36 470 **11. SIGNIFICANCE**

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38
39 471 A high rate of falling is a common after stroke, and fall risk is highest in the first months post-discharge
40
41 472 from rehabilitation.²³ RBT is a novel type of exercise that aims to improve reactive balance control,
42
43 473 rather than ‘traditional’ balance training, which focuses on maintaining stability during voluntary
44
45
46 474 movement. Time in stroke rehabilitation is limited, and physiotherapists report lack of time is a barrier
47
48 475 to implementing RBT.⁴¹ The results of the proposed study will inform the design of a larger RCT to
49
50 476 establish the optimal dose of RBT in sub-acute stroke. If a low dose of RBT can improve reactive
51
52 477 balance control and prevent falls post-stroke, this would allow therapists and patients to more easily
53
54
55 478 include this fall-prevention intervention in rehabilitation, without sacrificing time spent working on
56
57 479 other important rehabilitation goals.
58
59

1
2 480 **12. REFERENCES**

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2 586 **13. TABLES**3
4 587 **Table 1: Cohort descriptors and outcome measures.**
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	Study enrolment	Discharge	During six- month follow-up	6-months post- discharge
Demographics	✓			
Time post-stroke	✓			
Lesion location	✓			
Medical history	✓			
Medications	✓			
Changes in health/medications		✓		✓
NIH stroke scale ²⁷	✓			
Chedoke McMaster Stroke Assessment ²⁸	✓	✓		✓
Mini-Balance Evaluation Systems Test ²⁹	✓	✓		✓
Activities-specific Balance Confidence scale ³⁰	✓	✓		✓
Novel unpredictable perturbation	✓	✓		✓
Falls in daily life			✓*	
Physical Activity Scale for Individuals with Physical Disabilities ³⁷			✓*	
Subjective Index of Physical and Social Outcome ⁴²			✓*	

31 588 *Data collected repeatedly during the 6-month follow-up period.
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2 590 **14. FIGURE CAPTIONS**

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4 591 **Figure 1: Trial design.**

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For peer review only

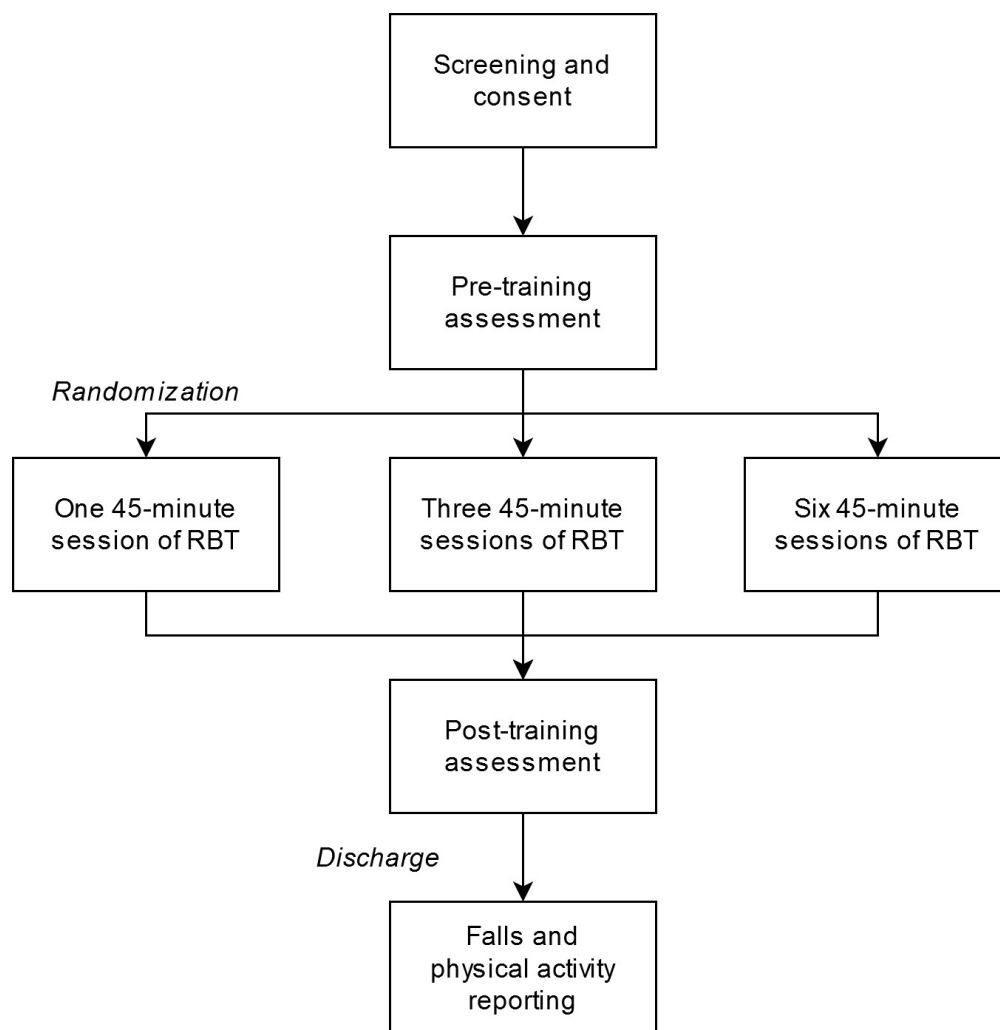


Figure 1: Trial design.

477x487mm (72 x 72 DPI)



CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Study title: Determining the optimal dose of reactive balance training after stroke – a pilot study

Principal investigator

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*Please note that communication via e-mail is not absolutely secure. Thus, please do not communicate personal sensitive information via e-mail.

Funding

This study is funded by the Heart and Stroke Foundation Canadian Partnership for Stroke Recovery.

IMPORTANT: You are being invited to take part in a research study. Before you agree to take part, it is important that you read the information below. The information describes the purpose of the study, the risks or benefits to you, and your right to withdraw at any time. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish including your friends, family, and family doctor. Participation in this study is voluntary.

Objective of the study

People who have had a stroke tend to have 'poor' balance and are more likely to fall than those who have not had a stroke. A new type of exercise, called 'reactive balance training', might help reduce fall rates after discharge from stroke rehabilitation. Some studies suggest that people can benefit from even small amounts of reactive balance training, but we do not know how much reactive balance training is necessary to improve balance and prevent falls. Our long-term goal is to determine the ideal number of reactive balance training sessions that will improve reactive balance control and prevent falls. We are currently conducting a small pilot study to determine the feasibility of a larger study to address this long-term goal.

You are being asked to participate because you have had a stroke within the last 6 months, you are attending outpatient rehabilitation at Toronto Rehab, and you are able to walk without assistance of another person.

Up to 36 people will participate in this study and it will take approximately 18 months to recruit all participants.

Study visits and procedures

If you agree to participate in the study, we will review your chart, you will complete balance training, we will test your balance and function, and we will ask you to report falls. The parts of the study are described below.

Chart review

We will review your hospital chart to get some information about your stroke, your previous medical history, and your current prescription medications. We use this information to confirm that you are eligible for the study and to describe the type of people who have participated in the study. You do not need to do anything additional for the chart review.

Reactive balance training

Reactive balance is the kind of balance that you need to stop yourself from falling after you stumble, trip, or get bumped, or jostled. Reactive balance requires you to step very quickly when you have lost your balance, to prevent a fall. In order for you to re-learn reactive balance, you need to lose your balance so that you can practice recovering with rapid steps. This is called **reactive balance training**.

Reactive balance training will be completed by your physiotherapist, and/or by a research physiotherapist. Reactive balance training is done in a safe, supportive, supervised environment. You will wear a harness which is attached to an overhead frame. The harness is worn so that when you lose your balance, you do not risk falling all the way to the floor. The physiotherapist will be there as well to assist you should you be unable to recover your balance on your own.

1
2 The physiotherapist will ask you to do exercises that cause you to lose your
3 balance. He or she will do this in one of two ways:

- 4 1. he or she will have you practice tasks that gradually challenge your balance
5 and result in a loss of balance, or
- 6 2. he or she will gradually pull or push you until you lose your balance.
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14 Images removed for publication
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20 **Example of task to challenge balance:** tapping
21 on unstable surfaces with alternating feet
22

23
24 **Example of 'pull' by
25 physiotherapist to left**

26 You will receive 1, 3, or 6 reactive balance training sessions; each session will be
27 45-minutes long and will replace 1, 3, or 6 of your regular physiotherapy
28 sessions. The timing of the sessions during your outpatient rehabilitation will be
29 determined by your physiotherapist.

30 *Balance and functional testing*

31 You will be asked to complete three testing sessions: 1) just before you start the
32 reactive balance training; 2) at the time of discharge from rehab; and, 3) 6-
33 months after you finish the training. Each testing session will last 2-2.5 hours.
34 The first session will be longer than the other two. You can take rest breaks as
35 often as you need during the testing sessions. During these test sessions, we will
36 ask you several questions and conduct several tests.
37
38

- 39 • Information about you (10 minutes) – we ask you some questions about
40 you and your life. We will ask questions about your employment, education
41 history, and social networks. We use this information to describe the type of
42 people who have participated in this study.
43
44
- 45 • Stroke function tests (20 minutes, first visit only) - we will do some quick
46 tests of your vision, memory, sense of touch, and arm and leg function.
47 These tests tell us how your stroke has affected you. We use this
48 information to describe the kind of people who participate in the study.
49
50
- 51 • Questionnaire (10 minutes) - we will ask you to complete a standardized
52 questionnaire about your balance confidence. We would like to know if
53 balance confidence improves after completing the training. You are free to
54 choose not to answer any of the questions. You can take the questionnaire
55 away with you and answer it at home if you like.
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- Leg and foot recovery (10 minutes) – we will ask you to do a few movements with your leg and foot that have been affected by the stroke, such as bending the knee or wiggling the toes. We would like to know if your ability to move the leg and foot improves after completing the training.
- Balance test (15 minutes) - we will ask you to do several activities that challenge your balance and mobility, such as walking as quickly as you can, standing with your eyes closed, and recovering your balance once released from a leaning position. A research assistant will stand near you when you complete the tests to provide any assistance you might need. The research assistant will rate how you perform on each test. We would like to know if your ability to perform these tests improves after completing the training.
- Balance reaction test (1 hour) - we will test your balance reactions on a movable platform. During this test, you will wear a safety harness attached to an overhead beam and you will be outfitted with reflective markers. We will ask you to walk forward on the platform 8-10 times. During 2 of the walking trials, the platform will move suddenly, requiring you to react to regain your balance. If you are unable to use your own balance reactions to prevent a fall, the safety harness will catch you. We would like to know if your balance reactions improve after completing the exercise program. Setting up for this test takes quite a bit of time, but the tests themselves will only take about 10-15 minutes.

All of the balance tests will be videotaped so that we can check out you performed the tests after you finish your appointment. The videotaping is mandatory for the study. Only study personnel will have access to your video images. We may ask for your permission to show the videos to some people outside the study (e.g., for educational purposes). We will ask you to provide this permission by signing a separate consent form, but you do not have to provide this permission. We will not share the videos with anyone outside of the study without your permission.

Falls reporting

We will ask you to complete a six-month falls monitoring period. When you have completed the assessment at the end of rehabilitation you will be provided with a calendar that you will be asked to fill out daily. You will use this calendar to record any falls or near falls that you experience. We will ask you to return the calendar to us every two weeks. If you experience a fall or a near fall, it is important that you get the medical care you may need. After your medical care is addressed, we will ask you (or a family member) to contact us to answer some questions about the fall or near fall. You can answer these questions over the telephone. The questions include what you were doing when you fell, what you think caused the fall, and whether you have a fear of falling. The questions should take 15-30 minutes to answer.

1
2
3 If you do not return a calendar we will call you to remind you to return it. We will
4 also call you three times during this six month monitoring period (about every 2
5 months) to ask you questions about your physical activities. These questions
6 should take about 15-30 minutes to answer.
7
8

9 **Study design**

10 This is an assessor blind pilot randomized trial.

- 11 • 'Assessor blind' means that the person who is collecting all of the
12 information for the study should not know which exercise program you are
13 in.
14
- 15 • 'Pilot' means a small study to test out the study procedures before planning
16 a larger study.
17
- 18 • 'Randomized' means that you do not have a choice of which group you are
19 in. You have an equal chance of being assigned to one of the three groups
20 and the assignment is decided randomly, like rolling a die.
21
- 22 • 'Trial' is another word for 'study'.
23

24 **Potential harms, discomforts and inconveniences**

25 This study involves being assigned to one of three different groups. One group
26 might do better than the other group. If you participate in this study you will get
27 the same or better standard of care than if you did not participate in the study.
28

29
30 There is some extra time involved with participating in this study. You will be
31 asked to do two assessments during outpatient rehabilitation that are 'in addition'
32 to your regular physiotherapy. You will be asked to travel to Toronto Rehab for
33 testing one time after your outpatient rehabilitation program is over; this will be
34 approximately 6 months after the end of the reactive balance training sessions.
35 You might find this a burden. If you require a family member to assist you with
36 transport they might also find that it is inconvenient to travel with you to the
37 study appointments.
38
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41 You might find the balance training or tests to be challenging or tiring. To
42 minimize the risk of physical harm, we do not allow people with certain medical
43 conditions to participate in this study. The sessions will be supervised by a trained
44 physiotherapist who will monitor you for any negative effects. You will be
45 provided regular rest breaks, and can request additional breaks. You can stop the
46 testing or training at any time if you are too tired to continue or are
47 uncomfortable. During the exercises and balance tests, there is a risk that you
48 will not be able to regain balance by yourself and will start to fall. You will wear a
49 safety harness to prevent you from falling to the floor. Additionally, the
50 researchers can help you to regain your balance. There is a very small chance
51 you will have an injury (such as a sprain or a bruise), even if you are caught by
52 the safety harness. However, we have done these types of tests and exercises
53 with hundreds of people with stroke without any injuries.
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1
2 If you agree to participate in this study you will have to fill out the falls
3 monitoring calendar every day and return it to us every two weeks. We will also
4 call you frequently to ask you questions about your falls and physical activities.
5 You might find that the calendars and the phone calls are inconvenient.
6
7

8 If you have difficulty understanding or speaking English you may need a family
9 member or friend to help you to participate in this study. They may need to
10 translate some of the study documents and questionnaires, speak to our research
11 personnel on the telephone. This may inconvenience your family member or
12 friend.
13
14

15 **Potential benefits**

16 If you participate in this study you will participate in reactive balance training. It
17 is possible that this training will benefit your balance.
18
19

20 The results of this study will give us more information about the amount of
21 training that is required to improve balance reaction. These results will be used to
22 inform the next research study and could be used in rehabilitation programs and
23 benefit other stroke patients in the future.
24
25

26 **Reminders and responsibilities**

27 It is important to remember the following things during the study:

- 28 • Tell the study staff your health history and medications as accurately as
29 possible. This will help to prevent any harm to you.
- 30 • Ask the study staff about anything that worries you.
- 31 • Tell the study staff if anything about your health has changed.
- 32 • Return the falls calendars regularly and report any falls to the study staff as
33 soon as possible.
34
35
36

37 **Alternatives to being in a study**

38 You do not have to join this study to receive treatment for your stroke. Your
39 outpatient rehabilitation program will be provided as scheduled.
40
41

42 **Confidentiality**

43 Your data will be shared as described in this consent form or as required by law.
44 All personal information such as your name, address, and phone number will be
45 removed from the data and will be replaced with a number. A list linking the
46 number with your name will be kept by the study investigator in a secure place,
47 separate from your file.
48
49

50 *Personal Health Information*

51 If you agree to join this study, the research team will look at your personal health
52 information and collect only the information they need for the study. Personal
53 health information is any information that could identify you and includes your:

- 54 • name,
- 55 • address,
56
57
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- age, and,
- new or existing medical records, that includes types, dates and results of medical tests or procedures.

Representatives of the University Health Network (UHN) including the UHN Research Ethics Board may look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study is following proper laws and guidelines.

The research team will keep any personal health information about you, including the videos, in a secure and confidential location for 10 years after we have finished collecting data for this study. All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law. You will not be named in any reports, publications, or presentations that may come from this study.

Research information in shared clinical records

If you participate in this study, information about you from this research project may be stored in your hospital file and in the UHN computer system. The UHN shares the patient information stored on its computers with other hospitals and health care providers in Ontario so they can access the information if it is needed for your clinical care. The study team can tell you what information about you will be stored electronically and may be shared outside of the UHN. If you have any concerns about this, or have any questions, please contact the UHN Privacy Office at 416-340-4800, x6937 (or by email at privacy@uhn.ca).

Alternatives to being in the study

The usual treatment for people with stroke at Toronto Rehab includes the treatment of balance when indicated. Your treatment will include all regular therapy programs as well as the addition of reactive balance training sessions.

Voluntary participation

You are encouraged to ask any questions that you may have about this study. If you do not wish to participate in this study it will not affect any treatment that might receive at Toronto Rehab or the University Health Network in the future. If you chose to participate initially but wish to withdraw at a later date, for any reason, it will not affect any future care that you receive at Toronto Rehab or the University Health Network. We will give you any new information about the study that might affect your decision to stay in the study.

Withdrawal from the study

If you choose to leave the study, the information that was collected before you left the study will still be used in order to help answer the research question. No new information will be collected without your permission.

Costs and reimbursement

You will be reimbursed for any travel expenses that result from the follow-up appointments. These travel expenses may include TTC fare, taxi fare, or parking. You will receive a \$50 gift card upon completion of the study.

Rights as a participant

If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.

By signing this form you do not give up any of your legal rights against the investigators, sponsor or involved institutions for compensation, nor does this form relieve the investigators, sponsor or involved institutions of their legal and professional responsibilities.

Conflict of interest

Researchers have an interest in completing this study. Their interests should not influence your decision to participate in this study.

Questions about the study

If you have any questions, concerns or would like to speak to the study team for any reason, please call Avril Mansfield at 416-597-3422 extension 7831. **If you have any questions about your rights as a research participant or have concerns about this study, call the Chair of the University Health Network Research Ethics Board (UHN REB) or the Research Ethics office number at 416-581-7849.** The REB is a group of people who oversee the ethical conduct of research studies. The UHN REB is not part of the study team. Everything that you discuss will be kept confidential.

You will be given a signed copy of this consent form.

Consent

This study has been explained to me and any questions I had have been answered.

I know that I may leave the study at any time. I agree to the use of my information as described in this form. I agree to take part in this study.

Study participant's name Signature Date

My signature means that I have explained the study to the participant named above. I have answered all questions.

Name of person obtaining consent Signature Date

Was the participant assisted during the consent process? YES NO

If **YES**, please check the relevant box and complete the signature space below:

The person signing below acted as an interpreter for the participant during the consent process and attests that the study as set out in this form was accurately interpreted has had any questions answered.

Name of interpreter Signature Date

Relationship to participant Language

The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to, and has had any questions answered.

Name of witness Signature Date

Relationship to participant



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Page no.
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	2-4
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	1
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	1
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	7
	6b	Explanation for choice of comparators	10
Objectives	7	Specific objectives or hypotheses	8

1				
2	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	8
3				
4				
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7				
8	Methods:			
9	Participants,			
10	interventions			
11	, and			
12	outcomes			
13				
14	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8-9
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20	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
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24	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10
25				
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29		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	9-10
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34		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	9-10
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39		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a
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41				
42	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-12
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51	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1 Table 1
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2	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
3				
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7	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	12-13
8				
9				

Methods: Assignment of interventions (for controlled trials)

Allocation:

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16				
17	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	13
18				
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26	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	13
27				
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33	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
34				
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37	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
38				
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41		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
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Methods: Data collection, management, and analysis

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51	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13
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2		18b	Plans to promote participant retention and complete follow-	13
3			up, including list of any outcome data to be collected for	
4			participants who discontinue or deviate from intervention	
5			protocols	
6				
7	Data	19	Plans for data entry, coding, security, and storage, including	14
8	management		any related processes to promote data quality (eg, double	
9			data entry; range checks for data values). Reference to	
10			where details of data management procedures can be	
11			found, if not in the protocol	
12				
13				
14	Statistical	20a	Statistical methods for analysing primary and secondary	14-15
15	methods		outcomes. Reference to where other details of the statistical	
16			analysis plan can be found, if not in the protocol	
17				
18				
19		20b	Methods for any additional analyses (eg, subgroup and	n/a
20			adjusted analyses)	
21				
22		20c	Definition of analysis population relating to protocol non-	n/a
23			adherence (eg, as randomised analysis), and any statistical	
24			methods to handle missing data (eg, multiple imputation)	
25				
26	Methods:			
27	Monitoring			
28				
29	Data	21a	Composition of data monitoring committee (DMC); summary	15
30	monitoring		of its role and reporting structure; statement of whether it is	
31			independent from the sponsor and competing interests; and	
32			reference to where further details about its charter can be	
33			found, if not in the protocol. Alternatively, an explanation of	
34			why a DMC is not needed	
35				
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38		21b	Description of any interim analyses and stopping guidelines,	n/a
39			including who will have access to these interim results and	
40			make the final decision to terminate the trial	
41				
42	Harms	22	Plans for collecting, assessing, reporting, and managing	16-17
43			solicited and spontaneously reported adverse events and	
44			other unintended effects of trial interventions or trial conduct	
45				
46				
47	Auditing	23	Frequency and procedures for auditing trial conduct, if any,	n/a
48			and whether the process will be independent from	
49			investigators and the sponsor	
50				
51	Ethics and			
52	dissemination			
53				
54	Research	24	Plans for seeking research ethics committee/institutional	17
55	ethics		review board (REC/IRB) approval	
56	approval			
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2	Protocol	25	Plans for communicating important protocol modifications	17
3	amendments		(eg, changes to eligibility criteria, outcomes, analyses) to	
4			relevant parties (eg, investigators, REC/IRBs, trial	
5			participants, trial registries, journals, regulators)	
6				
7	Consent or	26a	Who will obtain informed consent or assent from potential	17-18
8	assent		trial participants or authorised surrogates, and how (see	
9			Item 32)	
10				
11				
12		26b	Additional consent provisions for collection and use of	n/a
13			participant data and biological specimens in ancillary	
14			studies, if applicable	
15				
16	Confidentiality	27	How personal information about potential and enrolled	18
17			participants will be collected, shared, and maintained in	
18			order to protect confidentiality before, during, and after the	
19			trial	
20				
21				
22	Declaration of	28	Financial and other competing interests for principal	18
23	interests		investigators for the overall trial and each study site	
24				
25	Access to	29	Statement of who will have access to the final trial dataset,	18
26	data		and disclosure of contractual agreements that limit such	
27			access for investigators	
28				
29				
30	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for	19
31	post-trial care		compensation to those who suffer harm from trial	
32			participation	
33				
34	Dissemination	31a	Plans for investigators and sponsor to communicate trial	19
35	policy		results to participants, healthcare professionals, the public,	
36			and other relevant groups (eg, via publication, reporting in	
37			results databases, or other data sharing arrangements),	
38			including any publication restrictions	
39				
40				
41		31b	Authorship eligibility guidelines and any intended use of	19
42			professional writers	
43				
44		31c	Plans, if any, for granting public access to the full protocol,	18
45			participant-level dataset, and statistical code	
46				
47				
48	Appendices			
49				
50	Informed	32	Model consent form and other related documentation given	Appendix
51	consent		to participants and authorised surrogates	
52	materials			
53				
54	Biological	33	Plans for collection, laboratory evaluation, and storage of	n/a
55	specimens		biological specimens for genetic or molecular analysis in the	
56			current trial and for future use in ancillary studies, if	
57			applicable	
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1 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013
2 Explanation & Elaboration for important clarification on the items. Amendments to the
3 protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT
4 Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)"
5 license.
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For peer review only