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Protocol of a randomized controlled trial investigating the effectiveness of Recovery-focused Community support to Avoid readmissions and improve Participation after Stroke (ReCAPS)

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Abstract

Rationale: To address unmet needs, electronic messages to support person-centered goal attainment and secondary prevention may avoid hospital presentations/readmissions after stroke, but evidence is limited.

Hypothesis: Compared to control participants, there will be a 10% lower proportion of intervention participants who represent to hospital (emergency/admission) within 90 days of randomization.

Methods and design: Multicenter, double-blind, randomized controlled trial with intention-to-treat analysis. The intervention group receives 12 weeks of personalized, goal-centered, and administrative electronic messages, while the control group only receive administrative messages. The trial includes a process evaluation, assessment of treatment fidelity, and an economic evaluation. *Participants:* Confirmed stroke (modified Rankin Score: 0-4), aged ≥18 years with internet/mobile phone access, discharged directly home from hospital. *Randomization:* 1:1 computer-generated, stratified by age and baseline disability. *Outcomes assessments:* Collected at 90 days and 12 months following randomization.

Outcomes: Primary outcomes include hospital emergency presentations/admissions within 90 days of randomization. Secondary outcomes include goal attainment, self-efficacy, mood, unmet needs, disability, quality-of-life, recurrent stroke/cardiovascular events/deaths at 90 days and 12 months, and death and cost-effectiveness at 12 months. *Sample size:* To

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test our primary hypothesis, we estimated a sample size of 890 participants (445 per group) with 80% power and two-tailed significance threshold of $\alpha = 0.05$. Given uncertainty for the effect size of this novel intervention, the sample size will be adaptively re-estimated when outcomes for n = 668 are obtained, with maximum sample capped at 1100.

Discussion: We will provide new evidence on the potential effectiveness, implementation, and cost-effectiveness of a tailored eHealth intervention for survivors of stroke.

Keywords
Stroke, eHealth, self-management, healthcare technology, clinical trial protocol

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Introduction and rationale

Many survivors of stroke feel inadequately prepared for life back in the community with most reporting unmet needs.[1] Discharge planning should address the individual's needs with reference to their usual activities, home environment, personal concerns, and stroke risk.[2] Innovative, accessible, support, and education programs that align with survivor recovery and lifestyle goals are needed. Short message services (SMS) and eHealth tools have been proposed to support behavior change and disease management.[3] However, the effectiveness of tailored eHealth messaging for survivors after stroke has not been comprehensively assessed, with evidence limited to medication adherence, or to a subgroup of those with hypertension or depression.[4] In a recently published three-arm trial (n = 400) of a one-to-one facilitated intervention with a focus on "talking therapy" to improve self-management and quality of life in a similar population (*recently discharged directly to the community after stroke*), the intervention was shown to be effective.[5] This latter study provides some support for the need and potential effectiveness of patient-centered support programs after stroke, that has complementary elements to our approach.

We have co-designed the iVERVE (inspiring Virtual Enabled Resources following Vascular Events) intervention with leading stroke academics, clinicians, telecommunication engineers, and consumer representatives to establish an innovative, electronic self-management intervention, supporting person-centered goal attainment, and secondary prevention after stroke (see Supplemental file).[4] In our early Phase I randomized controlled trial (RCT) in people with chronic stroke, we had >80% retention, and acquired evidence to refine processes for goal-setting and assigning messages.[6] In Phase II, we tested the feasibility of this protocol (n = 37, completed 2019) to inform the final design of this Phase III RCT of the **Re**covery-focused **C**ommunity support to **A**void readmissions and improve **P**articipation after **S**troke (ReCAPS). This multicomponent intervention comprises: (1) standardized person-centered goalsetting (5 dimensions and 34 sub-items) and (2) personalized electronic messaging (>1300 available) tailored to the individualized goals.[6]

Methods

This is a prospective, parallel two-group, double-blind, multisite, Phase III randomized controlled trial with blinded outcome assessments and intention-to-treat analysis. The design includes a process evaluation, assessment of treatment fidelity, and an economic evaluation. Trial assessment periods (Figure 1) as well as baseline and outcome measures are outlined in Supplemental Table I.

Aims and hypotheses

The primary aim of the trial is to compare the effectiveness of ReCAPS to standard care in participants with stroke. The primary endpoint is the proportion of participants who present to hospital (emergency/admission) within 90 days of study randomization (Day 90) and the secondary endpoints include goal attainment, self-efficacy, mood, disability, and stroke/cardiovascular events/death. Cost-effectiveness will also be calculated.

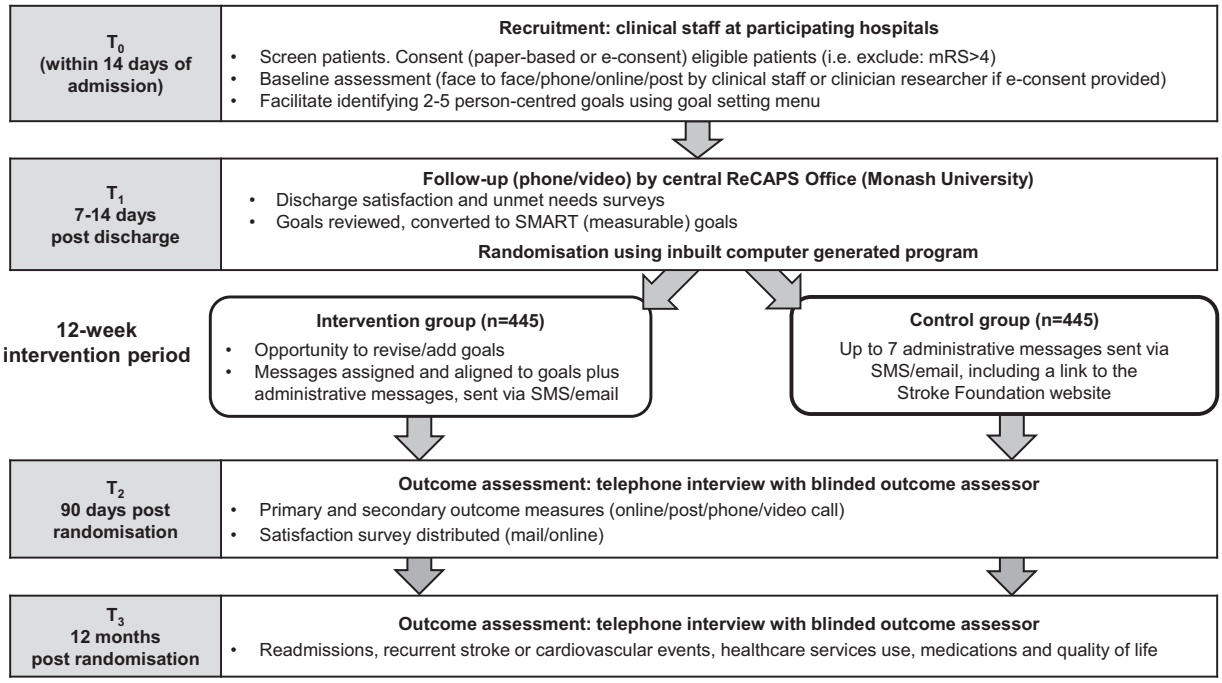
Primary hypothesis. Compared to control participants, there will be a 10% lower proportion of intervention participants who represent to hospital (emergency/admission) within 90 days of randomization.

Study population

Individuals admitted with acute stroke attending Australian public hospitals.

Inclusion criteria. Patients ≥18 years with capacity to consent, a confirmed diagnosis of stroke, discharged directly home within 10 to 14 days of admission, and a modified Rankin score[7] (mRS) 0–4. Patients require the ability to communicate in English and have access to, and use, the internet and/or smart phone technology.

Figure 1. Trial design. mRS: modified Rankin scale; ReCAPS: Recovery-focused Community support to Avoid readmissions and improve Participation after Stroke; SMS: short messaging service; SMART: Specific, Measurable, Achievable, Realistic, and Time-bound; T: Time/assessment.



Exclusions. Patients discharged to inpatient rehabilitation, those with an inability to communicate their goals, patients with a poor prognosis (<90 days), or requiring major surgery within 12 weeks of discharge.

Recruitment

Hospital clinicians from up to 16 hospitals will screen for eligibility, obtain consent, and collect baseline data. Participants are told that they will be randomly allocated to one of two groups and, to maintain blinding, details of the intervention are explained in general e.g., "you will receive one of the two support programs aimed at helping you after your stroke...and will involve you receiving information via SMS or email during a period of 12 weeks." Groups are not informed about the number of messages they can expect to receive and are unaware that only the intervention group have their messages tailored to their goals.

Trial procedures

Baseline assessments. Participants have their baseline assessments completed either in hospital, or shortly after discharge by phone, with the hospital clinicians or clinician researchers (Figure 1). All participants receive the same structured person-centered goal-setting procedure using the ReCAPS standardized goal-setting menu to identify between two and five goals to achieve over 12 weeks.

Randomization and blinding. Within 7–14 days of discharge, participants are contacted by a trained clinician researcher to complete a validated discharge satisfaction survey and unmet needs questionnaire (Supplemental Table I). The participant is then supported to restructure their stated goals to ensure they meet SMART requirements (Specific, Measurable, Achievable, Realistic and Time-bound),[8] if required. Once completed an affirmation to continue is requested, then online randomization (1:1 ratio) occurs using REDCap (Research Electronic Data Capture; a secure web-based data management system),[9] stratified by age (<65 or 65+ years) and disability (baseline mRS 0–2 or 3–4). In this manner, hospital clinicians are masked to group allocation as randomization occurs after discharge.

Intervention

Intervention components are summarized in Supplemental Table I. Participants review and prioritize their goals with the clinician researcher. They are given the opportunity to revise and add new goals to a

maximum of five, if original goals are no longer relevant. The responses from the unmet needs questionnaire may be used in revising or prioritizing participant goals, or in tailoring relevant messages. The SMS messages are then scheduled to be sent to participants using iVERVE,[4] commencing within 3–4 days and continuing over 12 weeks. Participants receive a message about using embedded hyperlinks in their messages to access relevant additional online information. Messages are aligned to each participants goal, and the priority specified by them. Messages are gradually introduced for each goal. In the first week, only messages related to their top priority goal are sent, and the number of messages sent over 12 weeks varies according to the number of goals. Intervention participants will receive between 4 and 7 personalized messages/week in addition to regular administrative and motivational messages about progress, equating to approximately one message/day. Participants are able to reply using a "STOP" message if they no longer wish to receive messages. They can also respond to questions in the messages or can ask questions/make comments[4] which are responded to within 72 hours by the research team.

Control arm

Participants are unable to add additional goals after baseline, but can drop an existing goal if no longer relevant. Consistent with the intervention group, they receive similar administrative messages. They also receive several administrative messages related to their follow-up appointments. The control group do not receive messages about using hyperlinks or receive messages of motivation about their progress. Both intervention and control groups receive a message in the first week with a link to the Stroke Foundation (Australia) website (https://strokefoundation.org.au/) for support.

Outcome assessments

Outcomes are collected at 90 days and 12 months from randomization via a scripted telephone conversation or video call with a trained research outcome assessor. To remain blind to participant group allocation, these outcome assessors are not involved in the telephone contact at 7–14 days. To facilitate the assessment, participants receive a copy of the health surveys, electronically or by post, one to two weeks in advance. All trial data are captured using REDCap[9] software.

Primary outcome. The primary outcome is the difference in the proportion of intervention and control group participants presenting to hospital (emergency department or admission) within 90 days of randomization. Hospital presentations are self-reported by participants, and verified from medical records and also validated using linked emergency and hospital administrative data held by government.

Secondary outcomes. These are assessed at 90 days and 12 months post-randomization and include standardized health outcome and resource-use measures including goal attainment, self-efficacy, anxiety and depression, hospital contacts, quality of life, education attainment, costs, and a composite outcome of recurrent stroke, cardiovascular events, or deaths (Supplemental Table I).

Data monitoring

An independent Data Safety and Monitoring Committee (DSMC) will review adverse events of interest (emergency presentations, falls, car accident(s) [i.e. if participant driving]) reported from consent to 90 days post-randomization. Serious Adverse Events (SAEs) will be reported for 12 months from time of consent. A medical monitor has been appointed to independently adjudicate SAE diagnoses and their relationship to the trial intervention.

Sample size

This effectiveness trial is powered to detect a 10% difference in the proportion of participants with a hospital presentation (emergency presentation/admission) within 90 days of randomization (34% versus 24%).[10] To achieve 80% power, with a significance threshold of $\alpha = 0.05$ two-tailed, we require 342 participants per group. This is a conservative estimate based on preliminary data from the Australian Stroke Clinical Registry (AuSCR) linked to hospital emergency and admissions data in four states (Victoria, New South Wales, Western Australia, and Queensland) and applying our study inclusion criteria.[11] To account for the possibility that up to 30% of participants may drop out, die, or decline consent to provide linked data for the emergency presentations/hospital admissions outcome, our pre-planned target sample size is 890 (445 per group). This sample size is also estimated to provide >80% power to detect statistically significant differences between groups for secondary outcomes including goal attainment. Nonetheless, given the indirect evidence used for the effect size, an adaptive sample size estimation procedure will be undertaken as per the "promising zone" methods of Mehta and Pocock[12] once the 90-day outcomes for $n = 668$ participants are obtained, with the maximum sample size capped at 1100.

Statistical analysis

A statistical analysis plan will be published before final data collection. A statistician blind to group allocation will oversee the data analyses.

Primary analysis. The primary outcome will be analyzed using intention-to-treat principles. To investigate whether the trial intervention reduces the proportion of participants with at least one hospital presentation (emergency presentation or admission) within 90 days post-randomization, we will use random effects logistic regression. The primary outcome will be the dependent variable, group allocation the independent variable, and hospital the random effect (*to account for potential heterogeneity in treatment effects*).

Secondary analyses. A per-protocol analysis is planned for those who completed 80% or more of the intervention to which they were randomized (i.e., remained in the study for at least 10 weeks). Descriptive statistics will be used to compare outcome measures for each group. Multivariable statistical models (as appropriate for the outcome measure, generalized linear, logistic, quantile or negative binomial regression) will be used. S*econdary outcomes* will be the dependent variables, group allocation the independent variable and the baseline scores for the *secondary outcomes* will serve as the covariates.

Missing data. Treatment of missing data will be based on the satisfying of missing at random assumptions, and will be based on the intention-to-treat strategy as per White et al.[13]

Process evaluation. A separate protocol for the process evaluation will be published. It will be based on the Medical Research Council guidance for complex interventions.[14] It will include researcher and hospital staff interview guides, and satisfaction survey analysis methods. The evaluation will capture fidelity to describe whether the intervention was delivered as intended.[14] The REAIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance) framework will be used when reporting process evaluation results.[15]

Economic evaluation. We will use a societal perspective that includes collecting data on direct health sector (hospitalizations, general practice, or allied health visits), out-of-pocket, and indirect costs associated with workforce participation or household productivity. Self-reported data are supplemented by obtaining participant consent to linked administrative data with hospitalizations, emergency department presentations, medical office visits, and medication dispensing records for 12 months before admission (to adjust for pre-stroke service use) and 12 months post-randomization. An incremental cost-effectiveness ratio (ICER) will be calculated as the net cost/Quality Adjusted Life Year (QALY; derived from the European Quality of Life-5 Dimensions EuroQoL-5D-3L[16] gained <$50,000 (willingness to pay threshold). Sensitivity and uncertainty analyses will be performed to assess the robustness of results.

Study organization and registration

ReCAPS is an investigator-initiated collaboration sponsored by Monash University. The trial is managed by an executive committee chaired by the principal coordinating investigator (author DAC). The DSMC is chaired by author GJH.

This trial is registered with Australian New Zealand Clinical Trials Registry (ACTRN12618001468213) and approved by Monash Health (2018-16435-22429) and Monash University (16435) Human Research Ethics Committee.

Discussion

This trial will provide important evidence on whether a personalized e-health support package for individuals discharged directly home after their stroke is effective in reducing hospital presentations. This five-year trial included a ''run-in'' feasibility component (Phase II) with 37 participants recruited from three hospitals. Processes and procedures were refined for the commencement of the Phase III trial with our first patient recruited in August 2019 and nine hospitals now having recruited over 200 participants by April 2021. COVID-19 has resulted in recruitment delays. To ensure timely recruitment of the necessary sample size, e-consent procedures have been established and we are in the process of onboarding four additional hospital sites. The process and economic evaluations will provide relevant information for the translation of our trial results.

Author's contributions

DAC (coordinating principal investigator), NEA, MFK, HMD, IK, AED, MH, NAL: conception and/or design; DAC, JC, NEA, MFK, IK, NAL: drafting the manuscript; all authors: critical review of the manuscript. All authors read and approved the final version of the manuscript.

Declaration of conflicting interests

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Supplemental material

Supplemental material for this article is available online.

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