Mass General Brigham

Institutional Review Board
Intervention/Interaction Detailed Protocol

Principal Investigator:	Amar Dhand, MD, DPhil
Project Title:	TEAMS-BP (The Enhancement of social networks to Augment Management of Stroke-Blood Pressure): A Randomized Control Trial
Version Date:	Version 17: March 27, 2024

1. Background and Significance

After ischemic stroke, blood pressure reduction is the most effective intervention to prevent recurrent stroke. Class I evidence suggests that the ideal blood pressure should be < 130/80.[1] However, maintaining this goal in real-world settings is challenging: one study suggested that only 42% achieved goal blood pressure at 1 year after stroke.[2]

Focus on the individual is common in the clinic and in research studies. Clinicians and researchers treat the patient as a solitary figure and the de facto unit of analysis. However, this is inconsistent with human nature.[3] Social network theory proposes that every patient is embedded in a social network of interpersonal connections that influence health outcomes.[4] Patients obtain information, social support, and behavioral cues through interpersonal contacts. In fact, there is a deep interdependence of social actors. Individual action is embedded in, and therefore continually affected by, preexisting ties between specific actors.[5] Built on trust and reciprocity, these social networks are conduits of health resources and behavioral patterns, particularly in diet, exercise, and other lifestyle habits.[4] Therefore, considering and leveraging social networks may be key strategy for addressing multi-dimensional behaviors. Indeed, ignoring them may be a key reason that behavioral interventions fail.[6]

The patient's personal social network is defined as the family, friends, and acquaintances who are inter-connected in a unique web of ties that may be quantified as a graph. The study team has created a REDCap-based instrument to measure patients' personal social networks for clinical research. Dr. Dhand and his colleagues have demonstrated that social networks are associated with outcomes in all phases of stroke care, including incident stroke,[7] rapid arrival to the hospital,[8] and recovery.[9]

Social networks could be leveraged to address hypertension control among post-stroke survivors for at least two reasons: 1) social networks influence and regulate the adoption of diet patterns, physical activity, and medication adherence, all of which are important to blood pressure management; 2) social network interventions relying on social support and social network education have been successful in blood pressure control in primary care settings.[10]

2. Specific Aims and Objectives

This proposed pilot project aims to leverage social networks to improve hypertension control for patients who have had an ischemic stroke. The study team hypothesizes that leveraging an individual's social network to monitor and treat blood pressure will more be more effective than a standard intervention to control post-stroke blood pressure. This study has the following Specific Aims:

Aim 1: To determine the effects of a social network intervention versus individual hypertension counseling on blood pressure control for patients discharged after ischemic stroke. In a pilot study, the study team will randomize 60 patients with ischemic stroke to 1) individual teaching, and 2) a social network intervention. The primary outcome will be the absolute reduction in systolic blood pressure at 3 months.

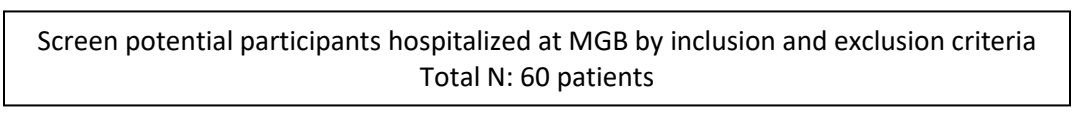
Aim 2: To determine the shortest questionnaire that maximizes network information important for the intervention. We will test whether a subset of our social network questionnaire is sufficient for information used in the network intervention. For the same participant, we will compare intervention-relevant network metrics (network size, proportion of network members who have hypertension) derived from the short version versus full version.

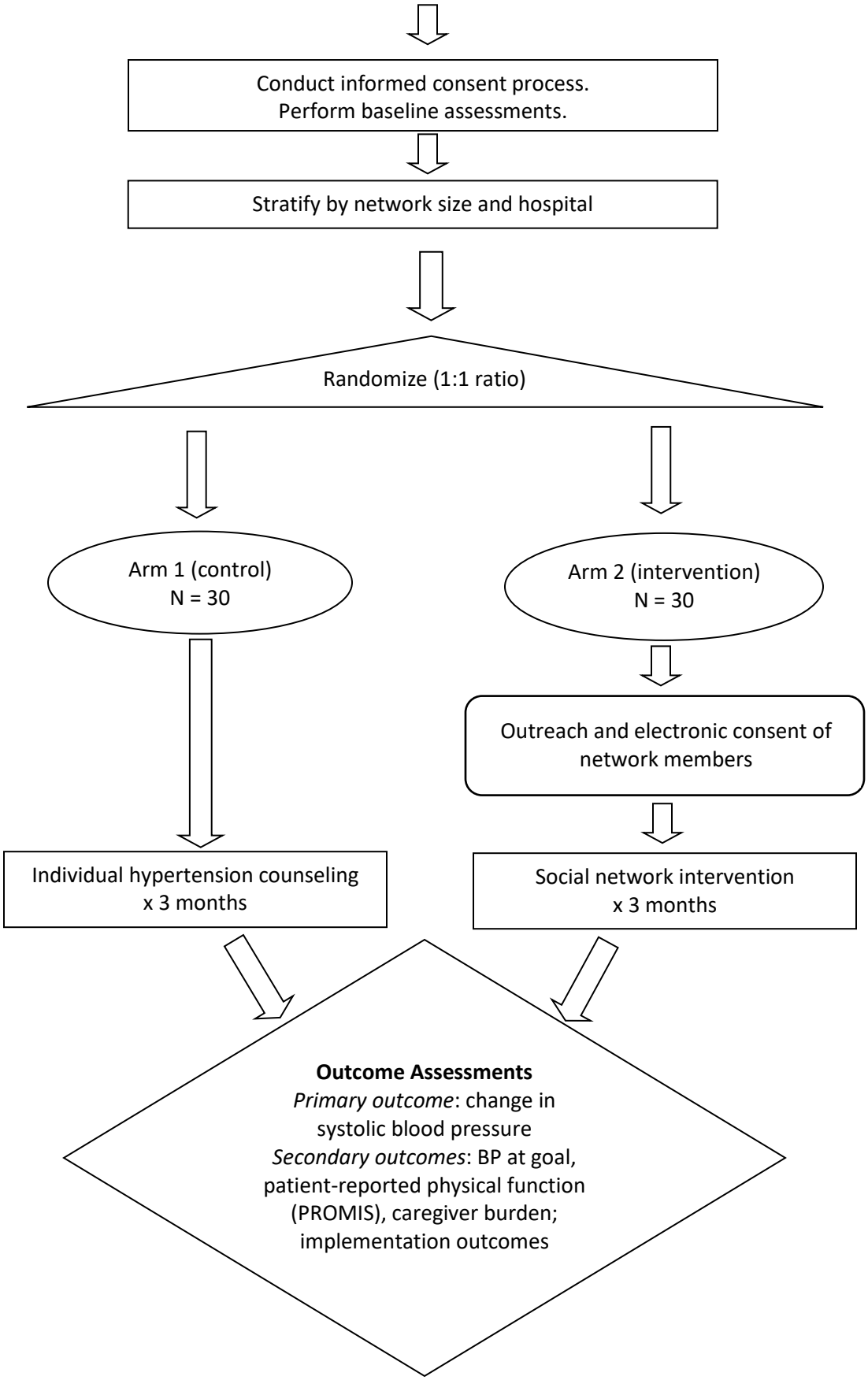
Aim 3: To understand the acceptability, adoptability, and mechanisms of the social network intervention. The study will explicitly evaluate implementation of the intervention by collecting and evaluating quantitative and qualitative data directly from patients and their networks.

3. General Description of Study Design

The study will enroll 60 patients hospitalized at Brigham and Women's Hospital, Massachusetts General Hospital and Spaulding Rehabilitation Hospital with a symptomatic and imaging-confirmed ischemic stroke and hypertension. During the index stroke admission, all enrolled patients' networks will be mapped using the validated PERSNET instrument.[11] Participants will then be stratified according to network size (<5 vs 5 or more) and location of hospitalization (MGH or BWH). Network size is the most potent network metric related to stroke recovery.[9] Patients in both arms will be administered blood pressure medications as needed during the hospitalization. Patients will then be randomized to receive individual hypertension counseling (control) or the social network intervention. In the individual hypertension counseling arm, patient networks will not be acted upon. The index patient will meet via Zoom three times over the course of 3 months with a clinical research nurse for blood pressure education. In the social network arm, the results of the PERSNET instrument will be used to identify the most influential network members based on their network position, driving distance from the patient, speaking frequency, and whether they have high blood pressure. Network members will then be contacted and consented for participation in the study. The index patient and consented network members will meet via Zoom for three visits over 3 months with a clinical research nurse for blood pressure education and teamwork coaching. The primary outcome of the study will be the absolute reduction in systolic blood pressure at 3 months follow-up.

3.1 Study Schema:




Conduct informed consent process.
Perform baseline assessments.
Stratify by network size and hospital
Randomize (1:1 ratio)
Arm 1 (control)
N = 30
Arm 2 (intervention)
N = 30
Outreach and electronic consent of network members
Individual hypertension counseling x 3 months
Social network intervention x 3 months
Outcome Assessments
Primary outcome: change in systolic blood pressure
Secondary outcomes: BP at goal, patient-reported physical function (PROMIS), caregiver burden; implementation outcomes

4. Subject Selection

4.1 INCLUSION/EXCLUSION CRITERIA:

4.1a Patient subjects

The study team will enroll 60 patients hospitalized at Brigham and Women's Hospital, Massachusetts General Hospital and Spaulding Rehabilitation Hospital with a symptomatic and imaging-confirmed ischemic stroke and hypertension.

Inclusion Criteria:

1. Acute ischemic stroke defined clinically with support from imaging if necessary
2. 21 years of age or older
3. History of hypertension or has been newly prescribed blood pressure medications during index admission
4. Within 14 days after stroke

Exclusion Criteria:

1. NIHSS > 21
2. Significant aphasia (Score>1 on the language section of the NIHSS)
3. Medical conditions for which death is likely within 6 months
4. Does not have capacity to consent for the project or participate in survey interview
5. Diagnosis of dementia
6. Patient has no phone or incapable of using text messages
7. Patient has opted out of participating in research noted within MGB Epic EHR system
8. Patient is on enhanced respiratory, airborne or contact plus precautions

4.1b Network subjects:

Inclusion Criteria:

Those people 18 years of age or older identified by patient-subjects randomized to the intervention (social network) arm during completion of the validated PERSNET instrument will be included.

Exclusion Criteria:

1. Participants who do not meet the defined inclusion criteria
2. Participant has no phone or are incapable of using text messages
3. Does not agree to participate

4.1c Exclusion of non-English speaking participants

We plan to exclude patient- and network-subjects who do not speak basic English, as the counseling component of the pilot intervention program and study-related text messages will be in English and the program does not have the ability to translate any non-English inputs. We plan to expand the language ability of the program, pending the success of this pilot program.

4.2 RECRUITMENT PROCEDURES:

4.2a Patient subjects

Similar to IRB approved study (Dhand, 2020P003739), the Research Assistants (RA) or other study staff will perform daily EHR screening of Brigham and Women's Hospital, Massachusetts General Hospital and Spaulding Rehabilitation Hospital inpatient admissions based on the study's inclusion and exclusion criteria listed above. If an inpatient meets criteria, study staff will inform the primary neurologist and nursing staff of a potential patient participant on their service and request their approval for the patient to be contacted for research purposes. Study staff will then request the patient's nurse to introduce the study to the patient and obtain the patient's permission to be contacted by study staff during their inpatient stay. Once permission has been obtained by both the nursing staff and patient, the study staff will approach the patient.

The RA/study staff will meet with the patient at bedside, explain the study to the patient, and ask their permission to make inquiries about their social network. Specifically, this study will recruit patients of all gender identities, as well as patients of all racial and ethnic backgrounds if they meet these criteria. Patients will not be excluded or differentially selected for the study based on race/ethnicity or gender. Women and minorities are well represented at MGB and in the eligible study populations.

4.2b Network subjects

A list of each consenting patient's most close-knit network members will be obtained during the baseline questionnaire completion (validated PERSNET instrument) and documented within REDCap. The most influential network members will be ranked based on their network position, driving distance from the patient, speaking frequency, and whether they have high blood pressure. Potential network members will be contacted initially by the patient and study team member to introduce the study to them. This will be done via phone call during the index patient's enrollment visit, in which the index patient will initiate the conversation and the study staff will follow a script for recruitment *(see "Network member phone recruitment script" attachment)*. If study staff are unable to get in touch with network members on first outreach, they will follow up with two additional phone calls on day 3 and day 10.

If the network member is interested in participation, they will be given the option to receive additional information and the study fact sheet via text message or email. The preferred method of outreach will be documented within REDCap, along with the appropriate email or phone number for contact.

- Network members who prefer **email outreach** will be read the following MGB-required warning language regarding unsecure email by study staff: *"The Mass General Brigham standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from Mass General Brigham. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, Mass General Brigham will not be held responsible. Your preference to receive unencrypted email will apply to emails sent from this research group/study only."* The study staff will then obtain verbal permission to send unencrypted email and document within REDCap prior to sending any unsecure email.
- Network members who prefer **SMS message** outreach will be read the following warning language by study staff: *"SMS texting is not a secure form of communication. Message and data rates may apply."* The study staff will then obtain verbal permission to send SMS texting and document within REDCap prior to sending any SMS outreach.

- Network members will indicate their preference for how they receive a copy of their signed consent form during the consent process. Participants will be able to choose to receive the consent through email or mail and provide the address to send the consent form to.

Network members will then be sent a text message or email with a link to an MGB-approved secure REDCap study fact sheet. If network members agree to participate upon review of the Fact Sheet, they will click "I agree" within REDCap. In line with the Tier II texting requirements articulated in the MGB Texting Patients and Research Subjects Guidelines, the study team will also specifically obtain consent from the patient and network members to communicate with them via texts that may contain some limited PHI. As required by these guidelines, patient and network participants will both receive a welcome message (after the initial consent has been obtained) that includes a statement that texting is not secure and requests the patient to respond "yes" or "y" to indicate their preference to continue to receive texts. Once a patient enrolls by responding "Y", a confirmation text will be sent that notifies them of the opt out process and discloses potential message and data charges the patient may incur (see "*Text message list"* attachment). If network members agree to participate over the phone but do not formally give their consent within REDCap, study staff will follow up with two additional messages, sent via the network member's preferred form of communication, 3 and 10 days after the initial outreach (see "*Network Member Recruitment Texts"* attachment).

5. Subject Enrollment

The study staff will obtain informed, written consent from all patients, and all network members will agree to participate using an electronic consent process through REDCap. Before being enrolled in the study, all participants will be required to give their consent to participate in the study. The RA/study staff will review either the written informed consent document (patient-subjects) or the study fact sheet (network-subjects) with all participants and answer any questions that they may have before the subjects agree to participate. Subjects will not be able to participate in any portion of the study before giving their written informed (patient) or electronic (network) consent.

5.1 PATIENT SUBJECT ENROLLMENT

The study staff will perform daily screening of hospital admissions based on the study's inclusion and exclusion criteria listed above. If an inpatient meets criteria, the study staff will directly approach the nurse, physician attending, or physician assistant who is caring for the patient to briefly explain the study and determine an appropriate time to meet with the patient. We will verify the inclusion and exclusion criteria with the treating provider. If permission is granted by the treating provider, the study staff will meet with the patient at bedside, explain the study to the patient, and ask the remaining exclusion criteria to confirm their eligibility. In particular, the study staff will confirm that the patient has a phone and is capable of sending and receiving text messages. Study staff will also ensure that patients are willing to engage network members in the study if assigned to the intervention arm. If the patient is interested in participating in the study, the study staff will then obtain informed consent from the patient using MGB-approved REDCap digital signature consent process, conduct baseline surveys, randomize the patient and, for intervention arm participants, collect contact information for their network members who will be directly contacted and invited to participate. Patients will be stratified according to network size (<5 vs 5 or more) and location of hospitalization (MGH or BWH), and then be randomized using a 1:1 ratio to receive individual hypertension counseling or the social network intervention.

Patients who are eligible for participation in this study and two other IRB approved studies led by Dr. Dhand (Dhand, 2020P003739 and 2020P000320) may be approached for participation in both studies within one enrollment visit. Study staff will explain both studies and emphasize that patients can choose to only participate in one of the studies. If interested, patients will be provided consent forms for both studies and will agree to participate in each study separately. Patients will then go through baseline questionnaires for both studies, completing any repeated questionnaires between both studies only once. Participation in the three studies will otherwise be separate.

Patient subjects will indicate their preference for how they receive a copy of their signed consent form during the consent process. Participants will be able to choose to receive the signed consent through email, mail or receive a hard copy while in the hospital. If they prefer to receive the consent through email or mail, they will provide the address to send the consent form to.

5.2 NETWORK SUBJECT ENROLLMENT

A list of each consenting patient's network members will be obtained during the patient baseline questionnaire completion as described above. The most influential network members will be ranked based on their network position, driving distance from the patient, speaking frequency, and whether they have high blood pressure. Network members able to participate in this study may include anyone identified by the study participant anywhere in the United States. Potential network members for the patient randomized to the intervention arm will be called by the patient along with study staff to introduce them to the study. If the network member is interested in participating, they will be sent a text message or email (per their preference and as detailed above in Section 4.2b) with a link to REDCap containing the study fact sheet for their review and electronic consent in which network members select "I agree" if they would like to participate.

We request a waiver of written documentation of informed consent for network members providing electronic consent. We believe this is justified for several reasons. First, this study presents no more than minimal risk to the network members seeing as their only task will be to join the counseling session and offer support to the patient. Further, the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. For this reason, the study team believes that a waiver of documentation of informed consent with an electronic Consent Fact Sheet including contact information to study staff and an opportunity to discuss questions/concerns will be the best consent process for network members participating in this study.

Additional network-subjects are allowed to join at any point throughout the 12-week study period, but only at the request of the index patient-subject. These additional members will be required to complete the consent process described above prior to being included in the Group SMS thread or being invited to participate in any of the study sessions.

6. STUDY PROCEDURES

6.1 Consent/Enrollment and Baseline Visit

The study staff will meet with the eligible patients at bedside, explain the study to the patient, and obtain written informed consent using MGB-approved REDCap digital signature consent process. The consent form will include consent for enrolled participants to receive follow-up outreach after

completion of the trial to participate in an implementation evaluation, to include either a brief survey or a brief qualitative interview. Study staff will then help the patient complete baseline questionnaires consisting of the validated PERSNET social networks questionnaire, stroke information, and the CES-D depression screen. Additional covariates, such as medication use, will be retrieved from the EHR. The PERSNET resulting network map will be used to identify network team members. Participants will then be randomized to either the Social Networks (intervention) arm or the Individual Counseling (control) arm. In the Individual Counseling arm, while the patient's network will be mapped, it will not be acted upon. In the Social Network arm, network members identified will be invited to participate in the study per the enrollment description above (Section 5.2). All patients will be provided with a wide-range blood pressure cuff (Medline MDS4001 blood pressure monitor) and instructions for weekly home monitoring. Patient will be asked to use this cuff to collect a baseline blood pressure measurement at the time of enrollment. A blood pressure measurement will also be collected from the patient's EHR on the day of discharge from the hospital. Finally, patients will be offered several Zoom meeting options and will schedule the first counseling session with study staff based on their availability.

Both this study and protocols 2020P003739 and 2020P000320 ask patients to complete the PERSNET social networks questionnaire. To simplify the enrollment process, patients that have consented to participate in both studies will only be asked to complete these questionnaires once for protocol 2022P000444. Data from these questionnaires will then be shared with protocols 2020P003739 and 2020P000320.

6.2 Between Study Visits

Upon enrollment of the patient-subject and their network members in the **Social Networks arm**, study staff will use an MGB-approved and properly configured study-specific cellular device to initiate a group SMS thread containing the index patient-subject, their consented network members (if applicable), and their assigned RA/study staff. This group SMS thread will be utilized for three types of communication: 1) appointment reminders from study staff, 2) facts/tips related to blood pressure control from study staff, and 3) organic correspondence between the patient and network members. Correspondence from study staff will be scripted (see *"Text message list"* attachment). Study staff will also collect email addresses from patients at baseline to use for back-up communication. Patients will be read the following MGB-required warning language regarding unsecure email by study staff: *"The Mass General Brigham standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from Mass General Brigham. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, Mass General Brigham will not be held responsible. Your preference to receive unencrypted email will apply to emails sent from this research group/study only."* The study staff will then obtain verbal permission to send unencrypted email and document within REDCap prior to sending any unsecure email. If necessary, study staff will follow up with patients over secure or unsecure email (per their preference) using the subject line "Follow-up for TEAMS-BP Study" if they are unable to make contact with the patient by phone after they are discharged from the hospital. All secure email communication will be sent using the SEND SECURE encryption mechanism and communication will resume on the cellular device if possible once contact has been made.

Upon enrollment of patient-subjects in the **Individual Counseling arm**, study staff will use an MGB-approved and properly configured study-specific cellular device to initiate an SMS thread with the

patient-subject. This SMS thread will be utilized for two types of communication: 1) appointment reminders and 2) facts/tips related to blood pressure control from study staff. Correspondence from study staff will be scripted (see *"Text message list"* attachment). Study staff will also collect email addresses from patients at baseline to use for back-up communication. Patients will be read the following MGB-required warning language regarding unsecure email by study staff: *"The Mass General Brigham standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from Mass General Brigham. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, Mass General Brigham will not be held responsible. Your preference to receive unencrypted email will apply to emails sent from this research group/study only."* The study staff will then obtain verbal permission to send unencrypted email and document within REDCap prior to sending any unsecure email. If necessary, study staff will follow up with patients over secure or unsecure email (per their preference) using the subject line "Follow-up for TEAMS-BP Study" if they are unable to make contact with the patient by phone after they are discharged from the hospital. All secure email communication will be sent using the SEND SECURE encryption mechanism and communication will resume on the cellular device if possible once contact has been made.

Upon initiation of the group SMS thread, study staff will send a text message with the date, time and Zoom meeting link for the first session based on the time agreed upon with the patient during the enrollment visit.

Text messages will only be read during regular business hours (Monday through Friday, 9AM – 5PM Eastern Time). Texts sent on nights, weekends or holidays will not be read until the following business day. If any participant sends a text message prompting a response to the study staff, the staff will respond utilizing minimum necessary MGB principles. For the following participant responses, automatic action will be taken with messages as follows:

Patient Response	**Automated action or text back to patient**
Stop	<Stop text messages>
Quit	<Stop text messages>
Thank you	You're welcome - keep up the good work!
Thanks	You're welcome - keep up the good work!
Ok	<No response>
<Response requiring medical attention>	This phone number is used for study purposes only and is not monitored by a licensed healthcare professional. If you need medical help, please contact your 24-hour nurse helpline, call 911, or go to your nearest ER.
<Other response>	<Minimum necessary response per MGB principles>

6.3 Counseling Sessions

All counseling sessions will take place remotely through Zoom, an MGB-approved secure video platform. In both the individual counseling and social network arm, participants will meet with the study nurse with an RA present on weeks 2,6, and 12 (+/- 7 days).

6.3a Counseling Session 1—On Week 2 (+/- 7 days)
The first counseling session will take place two weeks after initial enrollment. Study staff will ensure that only participants who have completed the consent process join the Zoom meeting.

Individual Counseling Arm
Patients in the individual counseling arm will meet individually with the study nurse. The nurse will provide counseling on the basics of blood pressure, taking and adjusting medications, monitoring blood pressure, reducing salt, and being physically active. The patients will then schedule their next session and collect a blood pressure measurement with cuff provided by the study staff under direct supervision by the nurse.

Social Network Arm
At the beginning of this session, the Research Assistant/study staff will confirm that all network-participants have completed the electronic consent process via REDCap.

The study nurse will begin the team-based counseling session in which she will provide counseling on teamwork and the same blood pressure control topics covered with the individual counseling group. The teamwork specific topics will include how networks can work together as a team, communication tips for engaging with one another and spreading positive messages and establishing the roles and responsibilities of each network team member. The team will schedule the following session and the patient will collect a blood pressure measurement with the cuff provided by the study staff under direct supervision by the nurse.

6.3b Counseling Session 2—On Week 6 (+/- 7 days)
The second counseling session will take place six weeks after initial enrollment. Participants in both arms will have received text messages every week in the three weeks between session 1 and session 2. Study staff will ensure that only participants who have completed the consent process join the Zoom meeting.

Individual Counseling Arm
Patients in the individual counseling arm will again meet individually with the study nurse who will review information about taking and adjusting medications, monitoring blood pressure, reducing salt, and being physically active. The patients will also collect a blood pressure measurement with cuff provided by the study staff under direct supervision by the study nurse.

Social Network Arm
Patients in the social network arm will again meet with their network members and the study nurse to review information about teamwork in the context of taking and adjusting medications, monitoring blood pressure, reducing salt, and being physically active that were covered in session 1. The nurse will work with the team for a revised plan, if necessary, to achieve optimal blood pressure by the final session. The patients will also collect a blood pressure measurement with cuff provided by the study staff under direct supervision by the study nurse.

6.4 End line Study Session—On Week 12 (+/- 7 days)

The third counseling session will take place twelve weeks after initial enrollment. Participants in both arms will have received text messages every week in the five weeks between sessions 2 and 3. Study staff will ensure that only participants who have completed the consent process join the Zoom meeting.

Individual Counseling Arm
Patients in the individual counseling arm will meet for a final time with the study nurse. In this session, the patient will check their blood pressure under direct video observation by the nurse. The nurse will also assess the study's secondary outcomes by taking note of the patient's blood pressure in relation to post-stroke hypertension treatment goal of <130/80 and the patient-reported physical function (based on the NIH PROMIS physical function sub-scale). Participants' social networks will be mapped to assess changes that may have occurred as a result of this study.

Social Network Arm
Patients in the social network arm will meet with their network team and the study nurse for a final time. In this session, the study nurse will first conduct a semi-structured interview with the patient and network members to assess the process and effectiveness of the sessions, as well as their views on their teamwork over the course of the intervention (see "*Interview Guide"* attachment). Prior to the interviews, subjects will be asked to provide verbal consent for audio recording of the interview. Patients will not be forced to participate and may withdraw their consent to participate at any time. Participants will be informed that participation is voluntary and that the interviews are part of the research study. The semi-structured interviews after the will be audio recorded, transcribed by the study team or by Landmark Associates (with whom MGB has a BAA agreement) and analyzed using qualitative software to identify themes using a grounded theory approach.

All network members will then be asked to leave the Zoom meeting, except for the primary caregiver (if applicable). The patient will collect a final blood pressure measurement under direct supervision of the study nurse, complete the PROMIS physical function scale, and remap their network with the PERSNET instrument to assess any changes that may have occurred as a result of the study. The primary caregiver network member will be asked to complete the caregiver burden scale which will be sent to them via a link in the Zoom chat or via text message.

Outcomes
The primary outcome of the study will be absolute reduction in systolic blood pressure at 3 months. Secondary outcomes will be attainment of a post-stroke hypertension treatment goal and patient-reported physical function. Feasibility measures will also be assessed throughout the intervention. End line caregiver burden will be measured in the social network arm compared to historical control data.

The intervention process evaluation conducted using semi-structured qualitative interviewing during the final session (Social Networks arm) will be analyzed using qualitative software to identify themes using a grounded theory approach. Once the data are analyzed, the investigators will review the findings to consolidate observations into a common set of themes.

Finally, a shortened version of the validated PERSNET utilizing only a subset of the initial questionnaire will be tested for predictive accuracy against the results of the full validated PERSNET scale.

6.5 Implementation evaluation

After the index patient completes their participation in the study, the study team may reach out to invite them to complete a survey or qualitative interview to determine implementation outcomes. Since this is a pilot study, we will also reach out to participants who have withdrawn from the trial in order to determine why they chose not to complete the behavioral trial. Questions in the implementation evaluation will include whether the patients found the timing of the intervention to be feasible or appropriate, whether they found the intervention to be helpful, how they felt about including network members in their recovery process, etc.

6.5 Data Collection Schedule

Time point	Individual Counseling Arm	Social Network Arm
Baseline (Week 0)	• Written consent • PERSNET • Demographics and stroke data (Age, Sex, Stroke severity, Charlston comorbidity index) • Blood pressure measure under direct observation	• Written consent • PERSNET • Demographics and stroke data (Age, Sex, Stroke severity, Charlston comorbidity index) • Blood pressure measure under direct observation • Network members contact info
Session 1 (Week 2 (+/- 7 days))	• BP measure under direct observation • Feasibility measures: number of participants, time of session, connection problems.	• BP measure under direct observation • Feasibility measures: number of participants, time of session, connection problems.
Session 2 (Week 6 (+/- 7 days))	• BP measure under direct observation • Feasibility measures: number of participants, time of session, connection problems.	• BP measure under direct observation • Feasibility measures: number of participants, time of session, connection problems.
End line (Week 12 (+/- 7 days))	• BP measure under direct observation • PERSNET • PROMIS • Feasibility measures: number of participants, time of session, connection problems.	• BP measure under direct observation • PERSNET • PROMIS • Caregiver burden (primary caregiver) • Intervention process evaluation (qualitative semi-structured interview) • Feasibility measures: number of participants, time of session, connection problems.
Upon completion of study (or after withdrawal)	• Implementation survey or qualitative interview	• Implementation survey or qualitative interview

6.6 Participant Remuneration

Patient-subjects will be remunerated for participation in the study. We plan to recruit 60 patients (30 intervention arm, 30 control arm), and all participation will be voluntary. Patients will receive $25 for completion of the first study session, $25 for completion of the second study session, and $50 upon completion of the final study session. Patient-subjects will receive this in the form of a single payment upon completion of study participation. Patient-subjects will also be able to keep the blood pressure cuff provided at the beginning of the study.

Network-subjects will not receive any remuneration for participation in the study.

7. Risks and Discomforts

The study team believes there is no more than minimal risk involved to the patient subjects for all phases of the research, as all medical decisions are ultimately made by their treating provider, and the study will follow best practices for maintaining confidentiality of study subjects involved. This study will also not interfere with the ordinary workings of clinical practices. All analyses and data provided to the study investigators will be based on anonymized, untraceable coded identifiers; this encryption eliminates the risk associated with an unlikely breach of confidentiality.

The main potential risk is a breach of confidentiality of the patient and their network members. Texting over mobile/cell phones carries security risks because text messages to mobile/cell phones are not encrypted. We are minimizing this risk by only transmitting mostly stroke prevention and hypertension control information, task adherence, and social skill education. Breach of this information should have minimal consequences, but the patient and network members will be informed of this risk during the consent process.

Protections Against Risk
To protect against the risk of inappropriate disclosure of personal health information, the investigators at BWH will only access study data with encrypted identifiers. As described, all members of the research team have completed or will complete appropriate human subjects research training and patient privacy training related to the Health Insurance Portability and Accountability Act (HIPAA). The study team has a history of collaborative evaluations with delivery organizations that involves transfer of the minimum data necessary to complete rigorous evaluations, involving the use of encrypted identifiers to ensure patient confidentiality.

To protect against risk associated with the use of a tablet device and SMS communication, the designated study-specific cellular device will undergo all provisions and configurations required by MGB Enterprise Mobility Management (EMM) and the Research Information Security Office (RISO).

To ensure the confidentiality and security of all data, the research team operates a secure, state-of-the-art computing facility housed at Mass General Brigham Healthcare's data center. The MGB data center is a secure facility that houses both computing environments as well as clinical systems and electronic medical records for several large hospitals in Eastern Massachusetts. Entry into the computer room requires staffed computer room security. The Division's computers are connected to the MGB networking backbone with 10 gigabit-per-second fiber links. Network security is overseen by electronic medical records systems to the research team's data. All data are transmitted to programmers' workstations in an encrypted state. Backups are created using 256-bit AES encryption, the current Department of Defense standard for data security, and are stored in a locked facility. The redundancy,

extensive data power, and security of the computer facility confirm the capacity to collect and manage data and ensure confidentiality for all project participants.

Any identifiable information will be safeguarded from the providers in accordance with IRB practices, limit access to any information in accordance with IRB practices, limit access to the information to study investigators actively involved in the research who have all undergone human subjects research training and destroy any recordings from the qualitative interviews upon completion of the research.

8. Benefits

Social network interventions may help increase treatment adherence for patients with uncontrolled hypertension after stroke. Thus, the research could have both immediate benefits for subjects enrolled in the study as well as for the larger populations of patients with poorly controlled hypertension. Several deliverables for this work will also be produced for the public, researchers, and policymakers, which will be shared as generalized knowledge. These deliverables include the results from the study, implementation toolkits, and the responsiveness profile characteristics.

9. Statistical Analysis

9.1 Statistical Hypothesis

The null hypothesis is that rates of systolic blood pressure change at 3 months will be equal in the intervention arm when compared to the control.

9.2 Power analysis

This pilot trial will be conducted for 12 months. In that time frame, the study team expects 1126 patients to be eligible across Brigham and Women's Hospital, Massachusetts General Hospital and Spaulding Rehabilitation Hospital (85% of all 1325 ischemic stroke patients given broad inclusion criteria). It is expected that ~20% of the patients will agree to participate based on prior experience of recruitment in this population. This creates a pool of 225 or 19 per month. Thus, the study team can feasibly recruit 60 patients within 4-5 months with buffer for unexpected issues.

Assuming a mean blood pressure of 150 +/- 13 points in the individual counselling arm and an alpha of 0.05, this study will need to enroll a total of 54 patients (i.e., 27 per arm) to have 80% power to detect a 10 mm Hg reduction blood pressure from the social network intervention. Therefore, planned enrollment of 60 should be sufficient power for this study to allow for loss to follow-up.

9.3 Statistical analysis

The primary outcome will be absolute reduction in systolic blood pressure at 3 months. Secondary outcomes will be attainment of a post-stroke hypertension treatment goal of <130/80 and patient-reported physical function (based on the NIH PROMIS physical function sub-scale). These outcomes will be evaluated, for intervention and control patients, on a 10-minute Zoom exit interview with direct observation on video by the study nurse.

Analysis will be conducted using intention-to-treat principles Evaluation of the primary outcome and physical function secondary outcome will be completed using linear controlling for any differences in baseline variables despite randomization. Logistic regression will be used for attainment of post-stroke hypertension treatment goal of <130/80 controlling for any differences in baseline variables.

For Aim 2, we will assess how a subset of questions in PERSNET predict the set of network members who were engaged in the intervention. We will calculate positive predictive value of the subset questions versus full network survey questions.

10. Monitoring and Quality Assurance

10.1 Adverse Events and Reporting

Oversight of the pilot will be the responsibility of the pilot PI: Amar Dhand, MD, DPhil. Dr. Dhand and study investigators will meet on a regular basis throughout the study period and will be in direct contact with the clinical study nurse conducting the intervention to obtain ongoing feedback. In addition, the protocol will undergo Institutional Review Board (IRB) evaluation.

De-identified study data will be accessible at all times for the BWH pilot PI and coinvestigators to review, if applicable. The study team will also ensure that all protocol deviations for the pilot study are reported to the NIH and the IRB according to the applicable regulatory requirements. Compliance of regulatory documents and study data accuracy and completeness will be maintained through an internal study team quality assurance process.

Definition:

Adverse Event (AE): Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

Adverse Events will be classified using the following rating scales:

- Severity: Mild, Moderate or Severe
    - Mild: Awareness of signs or symptoms but are easily tolerated
    - Moderate: Events introduce a low level of inconvenience or concern but may interfere with daily activities but are usually improved by simple therapeutic measures.
    - Severe: Events interrupt the participants' normal daily activities and generally require systemic drug therapy
- Expectedness: Unexpected or Expected
    - Unexpected: nature or severity of the event is not consistent with the condition under study.
    - Expected: event is known to be associated with the intervention or condition under study

Serious Adverse Event (SAE): Any adverse event that:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- Is another condition which investigators judge to represent significant hazards

Given the minimal risk nature of the study, in which the intervention involves enhanced education and monitoring of hypertension for patients at MGB, the PI does not expect any SAEs or AEs related to the information delivered in this trial.

Reporting:
As previously described, no SAEs or AEs are expected as part of this study, as the study team will not be providing any direct care to patients other than educational counseling received by a trained study nurse. All medical decisions will ultimately be made by the patient's medical team at MGB.

However, if the study team receives communication from MGB leadership or participants themselves and thus become aware of any AEs or SAEs throughout the course of the study, they will collect this information. Any reports of deaths will be submitted to the NIA Program Officer and to the Safety Officer (SO) within 24 hours. Any unexpected SAEs will be reported to the NIA PO, SO and the IRB within 48 hours of the study's knowledge of the SAE. All other reported SAEs and AEs received by the study team will be reported to the NIA Program Officer and to the SO quarterly.

10.2 Planned Safety Monitoring
General oversight of this project by the Brigham and Women's Hospital (BWH) pilot PI (Dr. Dhand) will occur throughout the study period, including regular contact with MGB clinical leadership involved in the project to obtain ongoing feedback. In addition, this protocol will undergo Institutional Review Board (IRB) evaluation. Dr. Niteesh Choudhry (co-investigator) has previously overseen numerous pragmatic trials.

This study will include safety monitoring from an independent safety officer (SO) to perform data and safety monitoring activities (**see Appendix A**). This SO will advise NIA Program staff and the PI regarding participant safety, study risks and benefits, scientific integrity, participant recruitment, and ethical conduct of the study.

Therefore, the pilot PI will appoint a designed individual with relevant study and disease-specific expertise to serve as SO, submitted to the NIA PO for approval. Following approval, the SO will receive a manual of operating procedures containing the study protocol and DSMP prior to study enrollment. The PI has nominated Avrum Gillespie, MD, as the independent Safety Officer (SO), pending approval by the NIA PO, to act in an advisory capacity to the NIA PO and to evaluate the progress of the study.

10.3 Frequency of Monitoring
De-identified study data will be accessible at all times for the BWH pilot PI (Dr. Dhand) and co-investigators to review, if applicable. The study team will also ensure that all protocol deviations for the trials are reported to the NIH and the IRB according to the applicable regulatory requirements. Dr. Dhand will also be in routine contact with other MGB clinical leadership to obtain any feedback from clinicians or patients regarding the study. Compliance of regulatory documents and study data accuracy and completeness will be maintained through an internal study team quality assurance process.
Safety reports are sent to the SO at least twice a year and will include a detailed analysis of study progress, data and safety issues.

11. Privacy and Confidentiality

☒ Study procedures will be conducted in a private setting

- ☒ Only data and/or specimens necessary for the conduct of the study will be collected
- ☒ Data collected (paper and/or electronic) will be maintained in a secure location with appropriate protections such as password protection, encryption, physical security measures (locked files/areas)
- ☐ Specimens collected will be maintained in a secure location with appropriate protections (e.g. locked storage spaces, laboratory areas) – N/A
- ☒ Data and specimens will only be shared with individuals who are members of the IRB-approved research team or approved for sharing as described in this IRB protocol
- ☒ Data and/or specimens requiring transportation from one location or electronic space to another will be transported only in a secure manner (e.g. encrypted files, password protection, using chain-of-custody procedures, etc.)
- ☒ All electronic communication with participants will comply with Mass General Brigham secure communication policies
- ☒ Identifiers will be coded or removed as soon as feasible and access to files linking identifiers with coded data or specimens will be limited to the minimal necessary members of the research team required to conduct the research
- ☒ All staff are trained on and will follow the Mass General Brigham policies and procedures for maintaining appropriate confidentiality of research data and specimens
- ☒ The PI will ensure that all staff implement and follow any Research Information Service Office (RISO) requirements for this research
- ☒ Additional privacy and/or confidentiality protections

Data for the study will be safeguarded by state-of-the-art security protocols. The facilities have 24-hour security and are protected by locked entrances. MGB has computer networks in place that employ up to date virus protection software and enable password protected access only to study investigators. The setup for analysis of these data will be the same as all the other IRB applications that the MGB research division submits for secondary use of data. All the datasets, including limited protected health information (PHI), will be stored only on secure servers at MGB's data center and will only be accessed by a limited number of individuals in the study team from this division who are all trained in data security and patient privacy.

To ensure the confidentiality and security of all data, the research team operates a secure, state-of-the-art computing facility housed at MGB's data center. The MGB data center is a secure facility that houses both computing environments as well as clinical systems and electronic medical records for several large hospitals in Eastern Massachusetts. Entry into the computer room requires staffed computer room security. The Division of Pharmacoepidemiology's computers are connected to the MGB networking backbone with 10 gigabit-per-second fiber links. Network security is overseen by electronic medical records systems to the research team's data. All data are transmitted to programmers' workstations in an encrypted state. Backups are created using 256-bit AES encryption, the current Department of Defense standard for data security, and are stored in a locked facility. The redundancy, extensive data power, and security of the computer facility confirm the capacity to collect and manage data and ensure confidentiality for all project participants.

The study team will also safeguard any identifiable information from the physicians in accordance with IRB practices, limit access to any information in accordance with IRB practices, limit access to the information to study investigators actively involved in the research who have all undergone human subjects research training.

All members of the research team have completed or will complete appropriate human subjects research training and patient privacy training related to the Health Insurance Portability and Accountability Act (HIPAA).

12. References

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8. Dhand, A. *et al.* Social networks and risk of delayed hospital arrival after acute stroke. *Nat. Commun.* **10**, 1206 (2019).
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APPENDIX A

Safety Officer

A Safety Officer (SO) will be convened for safety monitoring of this research study per determination of the National Institutes of Health. The following characteristics describe the SO for this study (Check all that apply):

☒ The Safety Officer is independent from the study team and study sponsor.

☒ A process has been implemented to ensure absence of conflicts of interest by the SO.

☒ The SO has the authority to intervene on study progress in the event of safety concerns, e.g., to suspend or terminate a study if new safety concerns have been identified or need to be investigated.

☒ Describe number and types of (i.e., qualifications of) members:
Name: Avrum Gillespie, MD
Title, Organization: Associate Professor of Medicine, Temple University
Dr. Gillespie is an expert in the study of social networks in nephrology. He has served as an investigator on the Systolic Blood Pressure Intervention Trial (SPRINT N01-HC-95258). Therefore, he has relevant expertise in social networks, hypertension, and clinical trial conduct that makes him qualified to serve in the role of safety officer.

☒ Describe planned frequency of meetings:
Per the NIA Notice of Award, recruitment is restricted until the SO has reviewed and recommended approval to NIA, with NIA's concurrence, the DSMP, IRB-approved study protocol, consent documents, and Manual of Operating Procedures.

Per the Data Safety Monitoring Plan, safety reports are sent to the SO at least twice a year and will include a detailed analysis of study progress, data and safety issues.

☒ SO reports with no findings (i.e., "continue without modifications") will be submitted to the IRB at the time of Continuing Review.

☒ SO reports with findings/modifications required will be submitted promptly (within 5 business days/7 calendar days of becoming aware) to the IRB as an Other Event.