HIC#2000023093

HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
(2017-1)

Protocol Title: Perioperative blood pressure screening to improve long-term cardiovascular health

Principal Investigator: Robert Schonberger, MD

Version Date: 01/31/2019

Clinicaltrials.gov Registration #: Pending

INSTRUCTIONS
This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:** 1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library. 2. If a section or question does not apply to your research study, type "Not Applicable" underneath. 3. Once completed, upload your protocol in the "Basic Information" screen in IRES IRB system.

SECTION I: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

   To explore in a pilot randomized clinical trial, the impact of Home Blood Pressure Monitoring with patient directed information as compared to usual care on the postoperative management of blood pressure.

   The intervention and control groups will be defined by, 1) preoperative home blood pressure monitoring with a detailed report sent to the patient, and 2) usual standard of care including a suggestion during the pre-operative clinic appointment to follow up with Primary Care. Both groups will receive a brief questionnaire about their blood pressure treatment and medication adherence. We will examine the rate of primary care follow-up and changes in hypertension treatment at 60 days post-operative, through a telephone call. This information, along with

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information regarding patient acceptance of the intervention will be used to inform the design of a future clinical trial powered to outcomes, including follow-up visits and blood pressure management.

2. Probable Duration of Project: State the expected duration of the project, including all follow-up and data analysis activities.

   Data collection will take approximately 12 months, with a 60-day post-surgical date follow up for all subjects. We estimate a 5-year time frame total, allowing for data collection and interpretation and publication after peer-reviews.

3. Background: Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

   Elevated blood pressure remains an important, and modifiable, cardiovascular disease (CVD) risk factor. Per the American Heart Association 2017 Hypertension Guidelines, "it was the leading cause of death and disability-adjusted life years worldwide" and, in the United States, it occupies first place for CDV deaths secondary to modifiable risk factors, and second place, after smoking, as a preventable cause of death for any reason.[1] Because of its preventable nature, we believe that as preoperative physicians, we have the opportunity to address and counsel patients that have elevated blood pressure, and potentially impact surgical and life-time outcomes.

   Randomized trials are the gold standard for the comparison of treatment effects but are resource intensive. Pilot studies can provide guidance for the formulation of such studies to ensure feasibility and the validity of the research plan.[2] We propose the following research plan.

4. Research Plan: Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable and include any flowcharts of visits specifying their individual times and lengths. Describe the setting in which the research will take place.

   In the proposed pilot study, we will recruit 100 preoperative patients in the preadmission testing center with blood pressure elevation for home blood pressure monitoring (HBPM) and questionnaires regarding life style and blood pressure treatment and adherence vs. usual care. Approximately 40% of our pre-operative population presents with a pre-surgical blood pressure > 140/90 mmHg. On the day of surgery, we will randomly assign patients with elevated home blood pressure into two groups comparing usual care with home blood pressure monitoring and feedback. We will then follow these patients to estimate the prevalence among the two groups of primary-care follow-up and new or adjusted hypertension treatment at 60-days post-surgery. To assess patient satisfaction with the interventions and medication adherence, a short questionnaire will be administered.

   Setting and population: We propose a pilot randomized trial that will take place at the preadmission testing center of YNHH, a Level 1 surgery center located within a large, diverse urban hospital that performs over 60,000 surgery cases per year. We expect to enroll 30 subjects each month and thus meet our recruitment goals within 3 months.

   Screening and Enrollment: Inclusion and screening: We propose to recruit patients who present for ambulatory surgery, aged >18 years, with a preoperative blood pressure > 140/90 mmHg taken as the mean of two readings during the pre-admission testing visit. Subjects must be able to speak on the phone and be able to provide their own consent. There will not be surrogate consent or surrogate participation in follow up phone visits. Patients who are unable or unwilling to be contacted by telephone, are non-English speaking, or are unable to operate an automated home blood pressure monitor will also be excluded.

Randomization: Individuals who meet the inclusion criteria and have provided consent to participate in the study will be randomized to one of two groups in a 1:1 ratio using permuted blocks of 4 and stratified by gender.

Interventions: While at the Preadmission Testing Center for their standard of care visit, all enrollees will complete a short questionnaire battery (please see Appendix I below for proposed survey) and be randomized to one of the two groups:

1) HBPM and Counseling group: Enrolled patients will be fitted with a HBPM device (Omron MX3 model BP742, Omron, Shaumberg, IL) and instructed in its use. The accuracy of this monitor has been validated previously.[3] For confirmation of device function and patient understanding, the patient will be asked to take two successive test readings. These will be compared to two successive readings taken by research personnel using a manual sphygmomanometer. If the average SBP or DBP readings differ by more than 10 mmHg, a new cuff/HBPM combination will be assessed. After validation, patients will be given the device to take home with instructions to record a series of two successive morning blood pressures and 2 successive evening blood pressures each day until their surgery date. Patients will be asked to return the HBPM device on the morning of surgery. At the same time they receive the HBPM device, they will also be provided with the National Institutes of Health (NIH) booklet called "Your guide on lowering blood pressure", which has several guidelines regarding diet, exercise and lifestyle changes that can be implemented to improve blood pressure control. After presentation for surgery and HBPM data processing, these patients will receive a summary report of the findings from their questionnaire and HBPM device feedback identifying whether they are likely to be able to control their hypertension (please see Appendix II below for proposed letters). If so, they will be instructed to follow-up in primary care within 30 days.
2) Usual Care Group: The usual care group will receive brief counseling after the PAT visit which will review their blood pressure readings taken at the clinic and how they compare with the American Heart Association (AHA) blood pressure guidelines. They will be offered the suggestion that they should follow up with their primary care doctor 2-4 weeks after their surgical episode is completed, or at their earliest convenience.

Assessments: All subjects will be contacted by telephone at 60 days postoperatively to ascertain (please see Appendix III below for proposed survey):

1. Subject's attendance at a primary care appointment within 60 days postoperatively.
2. New/adjusted treatment for hypertension within 60 days postoperatively.
3. Patient acceptance/satisfaction with blood pressure care.

5. Genetic Testing N/A ☒

6. Subject Population: Provide a detailed description of the types of human subjects who will be recruited into this study.

Patients will be recruited from the Pre-Admission Testing Clinic, both male and female, >18 years of age, English speaking and with a mean preoperative blood pressure $\geq$ 140 and/or 90 mmHg taken as the mean of two readings. They will be asked if they would like to participate in a pilot study that evaluates the impact on lifestyle modifications and blood pressure control after counseling provided in the pre-admission testing clinic. Patients who are agreeable will be referred to the PI or research personnel who will speak directly with them about the study and give a copy of informed consent. They will be recruited over a 3-month period and followed at 60-days after surgery.

Patients who are interested in counseling, but not in being randomized will receive the same counseling as the control group and will not be included in the study.

7. Subject classification: Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☐Children	☐ Healthy	☐Fetal material, placenta, or dead fetus
☐Non-English Speaking	☐ Prisoners	☐Economically disadvantaged persons
☐Decisionally Impaired	☐ Employees	☐Pregnant women and/or fetuses
☐Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes ☐ No ☒

8. Inclusion/Exclusion Criteria: What are the criteria used to determine subject inclusion or exclusion?

   Inclusion and screening: We propose to recruit patients who present for ambulatory surgery, both male and female, >18 years of age, and with a preoperative blood pressure ≥ 140 and/or 90 mmHg taken as the mean of two readings. Exclusion criteria: Non-English speaking patients, minors, patients unable to consent for themselves or refuse participation in the study, inability or unwillingness to be contacted by telephone, or an inability to operate an automated home blood pressure monitor.

9. How will eligibility be determined, and by whom?

   Dr. Diaz or designated research personnel, will be present in the preoperative clinic and will select patients who meet inclusion criteria and do not meet exclusion criteria. If the patient is alert, oriented and able to give self-consent, they will be asked to provide consent for participation. No surrogate consent will be accepted.

10. Risks: Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

    Bruising or discomfort from blood pressure cuff if fitted incorrectly or long measurement times due to elevated blood pressure values; possible subject anxiety or inconvenience over having to measure blood pressure twice daily.
    There may be a risk to privacy related to participation in research.

11. Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.

    a. Patients will be advised to rest and relax before the reading, and avoid activities known to influence BP such as caffeine, exercise, eating, talking or cold exposure 30 minutes before the measurement.
    b. We will ensure properly selected blood pressure cuffs based on patient physical characteristics, with a bladder length 80 percent of the patient's arm circumference, an ideal width of 40 percent, and a size selection as follows:
       - 22 to 26 cm 12 × 22 cm (small adult).
       - 27 to 34 cm 16 × 30 cm (adult).
       - 35 to 44 cm 16 × 36 cm (large adult).
    c. To reduce anxiety caused by blood pressure readings, we will reassure that these results will not affect their access to medical care or postpone their surgical treatment. We will also give more information about how accurate their elevated blood pressure in preadmission testing clinic really was and how this may be influenced by the clinical environment. We will also counsel patients on lifestyle modifications and follow up with their primary care physician.
    d. Regarding PHI, it will be stored for the shortest possible period of time and destroyed upon completion of data analysis. The minimal amount of PHI will be collected to conduct the study. Only de-identified information will remain on a server. For full discussion of storage and destruction of PHI, please see below.
    e. Every effort to minimize the risk to privacy will be taken by the research staff and clinicians including patient privacy protections that are standard of care, discussions in private exam rooms, and maintaining confidentiality about

research participation. All data collected as part of the study will be de-identified as soon as possible to protect privacy.

12. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal
    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? N/A
    c. Include an appropriate Data and Safety Monitoring Plan:

    The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency bi-weekly. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

    The principal investigator or the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

    This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project via email or in person. The protocol's IRB will be informed of any unexpected adverse events that carry implications for future subjects' decision to participate within 5 days of the event becoming known to the principal investigator.

    d. For multi-site studies for which the Yale PI serves as the lead investigator: N/A

13. **Statistical Considerations:** Describe the statistical analyses that support the study design.

    For the primary analysis, we will estimate the proportion of subjects with 90% confidence interval that had a primary care follow-up visit within 60 days and the proportion reporting new/adjusted hypertension treatment. For the primary analysis, we will consider those lost to follow-up as not receiving a primary care visit or new/adjusted hypertension treatment. We will also estimate the mean and standard deviation of the patient satisfaction score in each group.

    In secondary analyses, we will compare the proportion of patients in each group who received primary care follow-up and the proportion reporting new/adjusted hypertension treatment using the Fisher's Exact Test. The distribution in patient satisfaction scores will be compared among the two groups using a Kruskal–Wallis one-way analysis of variance by ranks test. In a further analysis, we will examine the proportion of patients demonstrating HBPM elevation. Specific cut-offs for the interpretation of home blood pressure are controversial.[4] For our own analysis, we will use the mean home blood pressure threshold $\geq$ 135/85 mmHg as indicating hypertension, in-line with recommendations from the American Heart Association.[2] A similar HBPM cutoff of 137/84 mmHg has previously been associated with a 10% increase in the adjusted relative hazard of mortality relative to ideal blood pressure.[5]

Sample Size: As the purpose of this pilot is to estimate the prevalence and distribution of outcomes and to assess feasibility, 100subjects will allow us to estimate for a continuous variable a 90% confidence interval around the mean of +/- 0.3 standard deviations. For the measurement of proportional outcomes, proportions of 0.10, 0.20, 0.30, and 0.40 will have 90% confidence interval widths of 0.21, 0.27, 0.30, and 0.32, respectively. These estimations will allow for a rigorous power analysis and sample-size estimation in future clinical trials.

Interpretation: The data from this pilot clinical trial will provide important information in constructing future interventions. Regarding feasibility, if significant non-adherence to the study protocol occurs, we may have to reconsider the nature of the intervention – perhaps moving toward a primary care provider-centered intervention that might result in improved adherence. In the event that adherence is high, implementing the proposed intervention in a larger cohort may gain acceptance from care providers and institutions more broadly. If the pilot demonstrates poor patient acceptance/satisfaction, the interventions will similarly be reexamined as above.

SECTION II: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, check off N/A and delete the rest of the section.

A. RADIOTRACERS ☒N/A

B. DRUGS/BIOLOGICS ☒N/A

B. DEVICES ☒N/A

SECTION III: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. Targeted Enrollment: Give the number of subjects:
   a. Targeted for enrollment at Yale for this protocol: 100
   b. If this is a multi-site study, give the total number of subjects targeted across all sites: Not applicable.

2. Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.

☐ Flyers	☐ Internet/web postings	☐ Radio
☐ Posters	☐ Mass email solicitation	☐ Telephone
☐ Letter	☐ Departmental/Center website	☐ Television
☒ Medical record review*	☐ Departmental/Center research boards	☐ Newspaper
☐ Departmental/Center newsletters	☐ Web-based clinical trial registries	☐ Clinicaltrails.gov
☐ YCCI Recruitment database	☐ Social Media (Twitter/Facebook):	
☒ Other: Referrals from Pre-admission testing center and chart review		

* Requests for medical records should be made through JDAT as described at http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx

3. Recruitment Procedures:

a. Describe how potential subjects will be identified.

Patients older than 18 years of age being seen at the preadmission testing clinic, will have two sets of blood pressure measurements, and, if at or above 140 and/or 90, they will be asked by the provider performing the PAT assessment if they are interested in learning more about the study. If they agree, they will be referred to Dr. Sofia Diaz or designated research personnel, who will discuss potential study participation with the patient.

b. Describe how potential subjects are contacted.

Potential participants will be seen in the PAT area after their appointment. If the patient expresses interest in learning more about the study, Dr. Diaz or designated research personnel will meet with the patient before they leave the PAT area to review the consent and establish eligibility.

c. Who is recruiting potential subjects?

Dr. Sofia Diaz or designated research personnel will be recruiting the patients who have a mean out of two blood pressures at or above 140 and/or 90, and express that they are interested in hearing more about this program.

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

☐Yes, all subjects

☒Yes, some of the subjects

☐No

If yes, describe the nature of this relationship.

The study investigators may provide anesthesia care to some of the subjects as part of their normal clinical responsibilities at YNHH.

5. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

Choose one: N/A

☐ For entire study

☒ For recruitment/screening purposes only

☐ For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data:
The investigators will look at participants' history of their hypertension treatment for the two years prior to their surgery, including any medications or other treatments for blood pressure that they may have been on previously or that they may be on now. We will approach only subjects who meet the appropriate inclusion criteria and therefore, will require a waiver of consent to review their blood measurement and name to approach them about the study. Written consent will be obtained if they are interested in study participation.

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data: *Write here*

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. Process of Consent/Assent: Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

   Consent will be provided to the interested patient in the Pre-Admission Testing Clinic. They will have the opportunity to read the consent form and ask questions in a quiet and private exam room. Dr. Diaz or designated research personnel will review the full Compound Authorization and Consent document with the subject discussing the purpose and scope of the study, explaining any risks and/or potential benefits, procedures associated with participation, economic considerations, confidentiality of the subject's information, and their ability to voluntarily participate and withdraw at any time during the study will be explained in person. It will be explained that participation is completely voluntary and that they may withdraw at any time without penalty. Full disclosure regarding their blood pressure measurement will be provided. Only after the patient has a thorough understanding of the study and what is being asked of them and after all their questions have been answered by the investigator or designated research personnel, will they be asked to indicate a decision to participate by signing the consent form. A copy of the signed consent form will be given to each subject.

7. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

   Patients participating should be alert and oriented, capable of clearly indicating their decision regarding participation or not, capable of paraphrasing the information provided, and show understanding of the risks, benefits and overall outcomes that can be expected from the pilot study.

8. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use. We do not plan to enroll any non-English speaking subjects at this time.

As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment? YES ☐ NO ☐

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. ***Please review the guidance and presentation on use of the short form available on the HRPP website.***

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. **Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study.** If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☐Not Requesting any consent waivers

☐Requesting a waiver of signed consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study (Note that an information sheet may be required.)

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☐ NO ☐
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☐ NO ☐

OR

- Does the research pose greater than minimal risk? YES ☐ NO☒
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☒

☒ Requesting a waiver of consent:

☒ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study

For a full waiver of consent, please address all of the following:

- Does the research pose greater than minimal risk to subjects?
  - ☐ Yes *If you answered yes, stop. A waiver cannot be granted.*
  - ☒ No
- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☒
- Why would the research be impracticable to conduct without the waiver? A waiver is necessary to pre-screen subjects by reviewing their medical record for blood pressure levels in order to avoid approaching those patients who do not meet inclusion criteria.
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date? *Write here*

SECTION IV: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

Health information collected at the initial visit includes full name, date of birth, gender, MRN, ASA status, type of surgery, date of surgery, current medication list and telephone number. Follow up for both groups at 60 days after date of surgery will be by phone. Data collected includes the initial and post-operative surveys (see attached appendix I and III). On the day of surgery, data from the HBPM group will be collected. Additionally, we will do a chart review post-operatively to look for blood pressure ranges following surgery.

2. How will the research data be collected, recorded and stored?

   Each patient will be assigned a number at time of initial visit. All patient information will be stored in a locked-box in the PAT clinic and uploaded on an encrypted, password protected computer. Patient data in the server will contain the assigned number, but will NOT contain MRN, patient's first name or any identified data. All paper sheets will be destroyed after being uploaded. A separate file with the key containing patient's first name, MRN, telephone number, day-of-surgery and assigned number will be used for day-of-surgery and telephone follow up's. This sheet will be stored on a separate iron-key encrypted flash-drive and will be password protected. This flash drive will be maintained by Dr. Diaz. Once all follow-up data is collected and de-identified information is uploaded, this file will be deleted per IT policy. All information gathered from follow-up will be uploaded onto the server, in a de-identified manner.

3. How will the digital data be stored? ☐CD ☐DVD ☒Flash Drive ☐Portable Hard Drive ☒Secured Server ☒Laptop Computer ☐Desktop Computer ☐Other

4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

   The use of locked boxes for paper information, de-identified information on a server for long-term data after final communication with the patient, use of minimal patient identifiers and software encryption (for sheets containing information for follow up and chart review) all help protect patient security.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

   Paper information in the locked box will be destroyed (shredded) once uploaded to the server. It will be destroyed by the study member uploading data to the server. The files containing patient name, MRN and telephone number will be destroyed (deleted digitally per IT policy) once the follow-up is complete by the study member performing follow-up interviews.

6. If appropriate, has a Certificate of Confidentiality been obtained? *N/A*

SECTION V: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

Subjects would benefit from lifestyle modifications that would ensure a healthier diet and increased physical activity. Diagnosis of high blood pressure with subsequent treatment can be obtained, as well as improved treatment or adherence to current treatment.

If these goals are accomplished by education and follow up by anesthesiologist at the perioperative clinic and by home blood pressure monitoring before surgery, an education protocol could be administered from perioperative clinics to decrease cardiovascular risk in patients with elevated blood pressure seen before surgery.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. Alternatives: What other alternatives are available to the study subjects outside of the research?

   Not taking part in the study.

2. Payments for Participation (Economic Considerations): Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

   There is no patient compensation for participation.

3. Costs for Participation (Economic Considerations): Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

   None.

4. In Case of Injury: This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws).

   The Primary intervention is not expected to cause any harm. It consists of discussion, information and questionnaires.
   a. Will medical treatment be available if research-related injury occurs? *No, no injuries related to participation are expected.*
   b. Where and from whom may treatment be obtained? *If the participant experiences any NRT related side-effects he/she should contact their primary care physician for assessment and instructions*
   c. Are there any limits to the treatment being provided? *N/A*
   d. Who will pay for this treatment? *Any medical treatment related to the use of NRT will be the patient's or his/her insurance.*
   e. How will the medical treatment be accessed by subjects? *Via their PCP*

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IMPORTANT REMINDERS

Will this study have a billable service? Yes ☐ No☒

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes ☐ No ☒

If Yes, please answer questions a through c and note instructions below.

a. Does your YNHH privilege delineation currently include the specific procedure that you will perform? Yes ☐ No ☐

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? Yes ☐ No ☐

c. Will a novel approach using existing equipment be applied? Yes ☐ No ☐

If you answered "no" to question 4a, or "yes" to question 4b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. **By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.**

APPENDIX I

Elevated blood pressure in the pre-admission testing clinic can be caused by several reasons including (but not limited to) anxiety, newly diagnosed hypertension, or diagnosed hypertension but issues with treatment. Because two of your blood pressure values were elevated today, we would like to ask you a few questions to better understand the possible cause behind this.

1. What is your gender?
   [ ] Female [ ] Male

2. What is your race?
   [ ] White/Caucasian [ ] Black/African American

   [ ] Asian [ ] American Indian/Pacific Islander

   [ ] Other

   And ethnicity?

   [ ] Hispanic/latino [ ] Non-hispanic/latino

3. Do you have a primary care physician (PCP)?
   [ ] Yes [ ] No

4. If yes, when did you last see your PCP?
   [ ] Less than a month ago [ ] 1-3 months ago [ ] 3-6 months ago
   [ ] 6-12 months ago [ ] More than one year [ ] I don't have a PCP

5. On a scale from 1 to 5, 1 being very difficult and 5 being very easy, how easy is it for you to get an appointment with your PCP when you need one?

   Very difficult Very easy
   ○ ○ ○ ○ ○

6. Has a doctor ever told you that you have high blood pressure?
   [ ] Yes [ ] No

7. If yes, how long ago were you told that you have high blood pressure?
   [ ] 0-6 months ago [ ] 6-12 months ago [ ] More than 12 months ago

8. Have you ever been in the emergency room or hospitalized for high blood pressure?
   [ ] Yes [ ] No

9. Has a doctor ever recommended or prescribed a treatment to lower your blood pressure?
   [ ] Yes [ ] No

10. If yes, what type of treatment? Select all that apply
    [ ] Diet changes [ ] Exercise
    [ ] Smoking cessation [ ] Medications

[ ] Stress management [ ] Home blood pressure monitoring

11. If you have a home blood pressure monitor, how often do you measure your blood pressure?
    [ ] Every day [ ] 1-3 times per week
    [ ] Every week [ ] 1-2 times per month
    [ ] A few times a year [ ] I don't have a home blood pressure cuff

12. If you take medications for your blood pressure, how many do you take?
    [ ] 1 [ ] 2 [ ] >=3

Extent of Adherence[9]

In order for blood pressure medication to work, people have to take it according to their doctor's instructions. For one reason or another, people can't or don't always take all of their pills as prescribed. We want to know how often you have missed your blood pressure medication. Please rate your agreement with the following statements.

Over the past 7 days…

1.	I took all doses of my blood pressure medication.	Strongly disagree ○ ○ ○ ○ ○	Strongly agree
2.	I missed or skipped at least one dose of my blood pressure medication.	Strongly disagree ○ ○ ○ ○ ○	Strongly agree
3.	I was not able to take all of my blood pressure medication.	Strongly disagree ○ ○ ○ ○ ○	Strongly agree

Reasons for Nonadherence[9]

Situations come up that make it difficult for people to take their blood pressure medications as prescribed by their doctors. Below is a list of those situations. We want to know how much these situations contributed to you missing a dose of your medication. Only one of these situations may apply to you, or many may apply to you.
In the past 7 days, how much did each situation contribute to you missing a dose of your blood pressure medication?

1. I was busy	Not at all ○ ○ ○ ○ ○	Very much
2. There was no one to remind me	Not at all ○ ○ ○ ○ ○	Very much
3. They caused some side effects	Not at all ○ ○ ○ ○ ○	Very much
4. I worried about taking them for the rest of my life	Not at all ○ ○ ○ ○ ○	Very much

5. They cost a lot of money	Not at all	○	○	○	Very much ○
6. I came home late	Not at all	○	○	○	Very much ○
7. I did not have any symptoms of high blood pressure	Not at all	○	○	○	Very much ○
8. I was with friends or family members	Not at all	○	○	○	Very much ○
9. I was in a public place	Not at all	○	○	○	Very much ○
10. I was afraid of becoming dependent on them	Not at all	○	○	○	Very much ○
11. I was afraid they may affect my sexual performance	Not at all	○	○	○	Very much ○
12. The time to take them was between my meals	Not at all	○	○	○	Very much ○
13. I felt I did not need them	Not at all	○	○	○	Very much ○
14. I was travelling	Not at all	○	○	○	Very much ○
15. I was supposed to take them more than once a day	Not at all	○	○	○	Very much ○
16. I had other medications to take	Not at all	○	○	○	Very much ○
17. They make me want to urinate while away from home	Not at all	○	○	○	Very much ○
18. I ran out of medication	Not at all	○	○	○	Very much ○
19. I was afraid the medication would interact with other medication I take	Not at all	○	○	○	Very much ○
20. My blood pressure was too low	Not at all	○	○	○	Very much ○

21. I was feeling too ill to take them	Not at all	○	○	○	○	○ Very much

APENDIX II

Healthy patient

Dear Mr./Ms. [patient name]

Congratulations! The following are your average home blood pressure measurements [BP mmHg], which are considered normal. We encourage you to continue with a healthy lifestyle to maintain these numbers, and to share these with your doctor.

As people age, their systolic blood pressures tend to rise so it is important to continue to monitor your blood pressures with your primary care physician from time to time in the future.

We wish you well, and a speedy recovery from your surgery.

Non-adherence (no HBPM letter)

Dear Mr./Ms. [patient name]

Based on your answers to our questionnaire, you are currently diagnosed with elevated blood pressure and receiving treatment. However, we noticed that when you were seen in our clinic, you had a blood pressure value that is considered elevated. We do not know whether your blood pressure is frequently elevated, but many patients with elevated blood pressure in our clinic have been shown to also have elevated blood pressures at home. Many patients sometimes find that it is difficult to take medications as prescribed, and when high blood pressure is untreated for a long period of time, it can increase your risk of bad health outcomes such as strokes, heart attacks, eye, and kidney problems.

We encourage you to follow up with your doctor to discuss your blood pressure medications and ways of helping to get your blood pressure under better control. We also encourage you to look at the enclosed brochure by the National Institutes of Health (NIH), which talks about ways you can help decrease your blood pressure through a healthy lifestyle. You can also obtain an electronic version at https://www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf

We wish you well, and a speedy recovery from your surgery.

Non-adherence (HBPM letter)

Dear Mr./Ms. [patient name]

The following are your average home blood pressure measurements [BP mmHg], which are considered elevated. Based on your previous answers to our questionnaire, you are currently treated for high blood pressure, but your blood pressures remain elevated. One common reason for this is that sometimes it is difficult to take your medications as prescribed. When high blood pressure is untreated for a long period of time, it can increase your risk of bad health outcomes such as strokes, heart attacks, eye, and kidney problems.

We encourage you to follow up with your doctor to discuss your blood pressure medications and ways of helping to get your blood pressure under better control. We also encourage you to look at the enclosed brochure by the National Institutes

of Health (NIH), which talks about ways you can help decrease your blood pressure through a healthy lifestyle. You can also obtain an electronic version at https://www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf

We wish you well, and a speedy recovery from your surgery.

Non-diagnosis (no HBPM letter)

Dear Mr./Ms. [patient name]

Based on your answers to our questionnaire, you have never been diagnosed with high blood pressure. However, we noticed that when you were seen in our clinic, you had a blood pressure value that is considered elevated. We do not know whether your blood pressure is frequently elevated, but many patients with elevated blood pressure in our clinic have been shown to also have elevated blood pressures at home.

We encourage you to speak with your primary care doctor about your blood pressures. Some people measure their blood pressures at home to help determine whether they need treatment or not.

We have also included a brochure by the National Institutes of Health (NIH), which talks about ways you can help decrease your blood pressure through a healthy lifestyle. You can also obtain an electronic version at https://www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf

We wish you well, and a speedy recovery from your surgery.

Non-diagnosis (HBPM letter)

Dear Mr./Ms. [patient name]

The following are your average home blood pressure measurements [BP mmHg], which are considered elevated. Based on your previous answers, you have never been diagnosed with elevated blood pressure. However, we noticed that when you were seen in our clinic, you had a blood pressure value that is considered elevated. After you went home, your average blood pressures remained elevated at home. When high blood pressure is untreated for a long period of time, it can increase your risk of bad health outcomes such as strokes, heart attacks, eye, and kidney problems.

We encourage you to follow up with your doctor to discuss your blood pressure results from this letter and to discuss ways of helping to get your blood pressure under better control. We also encourage you to look at the enclosed brochure by the National Institute of Health (NIH), which talks about ways you can help decrease your blood pressure through a healthy lifestyle. You can also obtain an electronic version at https://www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf

We wish you well, and a speedy recovery from your surgery.

Treatment Inertia (no HBPM letter)

Dear Mr./Ms. [patient name]

Based on your answers to our questionnaire, you are currently being treated for high blood pressure. We do not know whether your blood pressure is frequently elevated, but many patients with elevated blood pressure in our clinic have been shown to also have elevated blood pressures at home.

We encourage you to speak with your primary care doctor about your blood pressures. Some people with high blood pressures may need to intensify their treatment, and many patients measure blood pressures at home to help figure out what treatments work best.

We have also included a brochure by the National Institutes of Health (NIH), which talks about ways you can help decrease your blood pressure through a healthy lifestyle. You can also obtain an electronic version at https://www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf

We wish you well, and a speedy recovery from your surgery.

Treatment Inertia (HBPM letter)

Dear Mr./Ms. [patient name]

The following are your average home blood pressure measurements [BP mmHg], which are considered elevated. Based on your previous answers to our questionnaires, you are currently treated for high blood pressure. However, we noticed that when you were seen in our clinic, you had a blood pressure value that is considered elevated. After you went home, your average blood pressures remained elevated at home. When high blood pressure is untreated for a long period of time, it can increase your risk of bad health outcomes such as strokes, heart attacks, eye, and kidney problems.

We encourage you to speak with your primary care doctor about your blood pressures. Some people with high blood pressures may need to intensify their treatment, and many patients measure blood pressures at home to help figure out what treatments work best.

We have also included a brochure by the National Institutes of Health (NIH), which talks about ways you can help decrease your blood pressure through a healthy lifestyle. You can also obtain an electronic version at https://www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf

We wish you well, and a speedy recovery from your surgery.

APENDIX III

60-day post-operative questionnaire

When we saw you in our preadmission testing clinic, you were found to have two elevated blood pressure readings. Because of this you agreed to be enrolled in a pilot trial regarding lifestyle, habits and blood pressure management modifications. We would now like to ask you some questions regarding these subjects and your satisfaction with the whole process.

1. Have you seen your primary care physician since your surgery?

   [ ] Yes [ ] No

If yes, and A) On medications, continue to question 3; or B) On no medications, continue to question 5.

If no to this or any of the following questions, continue to question 6.

2. Did you and your doctor discuss blood pressure treatment during that appointment?

   [ ] Yes [ ] No

3. Have you had any changes in your blood pressure treatment since your surgery?

   [ ] Yes [ ] No

4. If yes, what changes?

   [ ] Increase in dose [ ] Change in medication [ ] Addition of medication

5. Have you received any new medicines to treat your blood pressure since your surgery?

   [ ] Yes [ ] No

6. You may remember that we gave you a brochure about blood pressured a healthy lifestyle before you came for surgery. Have you taken any steps to control your blood pressure?

   [ ] Yes [ ] No

7. If yes, which of the following (select all that apply):

   [ ] Diet changes [ ] Exercise
   [ ] Smoking cessation [ ] Medications
   [ ] Stress management [ ] Home blood pressure monitoring

The following are questions regarding your satisfaction with this project. On a scale from 1 to 5:

1.	How satisfied are you with your participation in our blood pressure study?	Not at all	○	○	○	○ Very much ○
2.	How easy was it for you to take your home blood pressures for the study?	Not at all	○	○	○	○ Very much ○
3.	How helpful was the brochure that you received in helping you understand the importance of blood pressure control?	Not at all	○	○	○	○ Very much ○
4.	How helpful was the follow-up visit on the day of surgery to discuss you home blood pressure monitoring readings?	Not at all	○	○	○	○ Very much ○

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