Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR
Rory B. Weiner MD, Division of Cardiology, Cardiac Ultrasound Laboratory.

PROTOCOL TITLE
An Educational Intervention to Improve Appropriate Ordering of Echocardiograms on the Outpatient Internal Medicine and Cardiology Practices.

FUNDING
Internal

VERSION DATE
07/30/13

SPECIFIC AIMS
Concisely state the objectives of the study and the hypothesis being tested.

1. To determine if an educational and feedback intervention based on the American College of Cardiology (ACC) Appropriate Use Criteria (AUC) for echocardiography will result in reduced ordering of inappropriate transthoracic echocardiograms by attending cardiologists and internists.

BACKGROUND AND SIGNIFICANCE
Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

In response to increasing utilization of echocardiography, the American Society of Echocardiography along with the American College of Cardiology released Appropriate Use Criteria (AUC) for transthoracic echocardiography (TTE) in 2007, and these have been subsequently updated in 2011. TTE ordering patterns have been evaluated and have shown that between 15-30% of TTE ordered are inappropriate. The highest rate of inappropriate TTE is found in the outpatient environment, where routine or “surveillance” studies are common. These studies have also found that internists and cardiologists order the majority of TTE. We previously documented that an AUC-based educational and feedback intervention reduced the rate of inappropriate TTE by cardiology and internal medicine physicians-in-training.
Whether this type of intervention can improve TTE ordering of attending level physicians is not known.

**RESEARCH DESIGN AND METHODS**

| Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, “Enrollment at Partners will be limited to adults although the sponsor’s protocol is open to both children and adults.” |

Internal medicine physicians in the Internal Medicine Associates and the Bulfinch Medical Group and Cardiology attending physicians will be recruited to participate in this study. After written consent from each physician is obtained, the physicians will be randomized into two study arms: 1) a control arm; 2) intervention group that receives one 30 minute educational session on AUC for TTE at the start of the study, a pocket card detailing common ordering indications, and a monthly feedback report on TTE ordering, including total number of TTEs ordered during the month, the number of inappropriate TTEs ordered, and reasons why the inappropriate TTEs were classified as such.

Echocardiogram “appropriateness” will be evaluated using the 2011 AUC, and 2 study investigators will independently determine the appropriateness of each test. We will enroll approximately 150 physicians, who will be divided into control and intervention groups by a random number generator.

This same methodology was utilized for our previous study of cardiology fellows and internal medicine residents. That study showed a reduction in the number of inappropriate TTEs in the intervention arm.

The study period will be 12 months. The proposed start date is later Fall 2013. The study endpoints include the total number of TTEs ordered, the number of inappropriate TTEs ordered by each study arm, and a results of a 5 question quiz given to all team members in each study arm testing knowledge of AUC and collecting information on attitudes toward diagnostic testing.

| Briefly describe study procedures. Include any local site restrictions, for example, “Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study.” Describe study endpoints. |

See above. No local site restrictions.
For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

Currently, ordering a TTE on a patient is done at the discretion of the ordering physician. This is a paper based system that does not include any decision support tools.

The study procedure does not change the ability of a physician to order a TTE study on a patient, whether considered inappropriate by the AUC or not. This intervention provides an educational session pre-study period and feedback to the physician on his/her ordering behavior. There are no punitive consequences for physicians based on their ordering behavior and the individual feedback reports will not be shared with any of their site directors or direct supervisors. Thus, the intervention should not adversely impact the standard of care for patients at MGH and does not impact the ability of physicians to order diagnostic tests on their patients. In fact, the intervention will serve as an educational tool that will enhance the physicians’ understanding of the appropriateness criteria for echocardiography.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

See above.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

The study protocol uses only non-invasive cardiac imaging with minimal inherent risk to patients. The TTEs will be ordered for clinical reasons and would be performed on patients regardless of this study. The study protocol does not limit the ordering of TTEs by the study physicians and there are no punitive consequences to ordering behavior.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.
There are no appreciable risks of transthoracic echocardiography. There is the potential that participants in the intervention arm may hesitate to order TTEs or under-order TTEs to improve their performance results. This may result in under-ordering of appropriate TTEs. However, the study protocol does not limit the ordering of TTEs by the study physicians and there are no punitive consequences to ordering behavior. In addition all ordering results will be confidential and not shared with the site directors or direct supervisors, thus the risk to under-ordering of inappropriate studies are low. In cases where a physician may be unsure of the indication to order a TTE study, both intervention arms will be able to contact a cardiologist associated with the study to receive guidance. As above, this methodology was successfully utilized in a study of cardiology fellows and internal medicine residents.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, “It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects.” Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

There is unlikely to be harm to individual patients, and the benefit to individual patients may be in avoidance of unnecessary testing.

There primary benefit of this study is the testing of an educational tool to reduce the ordering of inappropriate TTEs in the ambulatory environment. Reduction in inappropriate TTEs may lead to improved Echocardiography resource utilization and reduction in costs. Results of this study will provide a tool that may be tested in other healthcare settings. The results of this study may provide further evidence of non-punitive performance measurement and feedback as a tool to change physician behavior.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

This is not applicable in this study.
When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

This is not applicable in this study.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
http://healthcare.partners.org/phsirb/nonengco.htm

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

Recruitment of study participants will be based on physicians practicing in the above defined Internal Medicine practices and the Cardiology Division at MGH. All physicians will be asked to provide verbal consent prior to participation. Methods to increase recruitment methods for women and minorities are not applicable.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available.

No remuneration for study participants will be provided.

For guidance, refer to the following Partners policies:
Recruitment of Research Subjects
http://healthcare.partners.org/phsirb/recruit.htm

Guidelines for Advertisements for Recruiting Subjects
http://healthcare.partners.org/phsirb/advert.htm

Remuneration for Research Subjects
http://healthcare.partners.org/phsirb/remun.htm
CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators’ own patients, describe how the potential for coercion will be avoided.

Verbal consent after distribution of a fact sheet, under supervision by a member of the study investigation team, will be obtained from each physician. Approval by the Internal Medicine practice directors and the Chief of Cardiology will be obtained prior to proceeding with the study protocol.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website: http://healthcare.partners.org/phsirb/newapp.htm#Newapp

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects
http://healthcare.partners.org/phsirb/infcons.htm

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

All data will be reviewed by the principal investigator and one other investigator in the study. Aggregated, anonymous data will be shared at the 3 month and 6 month mark with the Internal Medicine site directors and Chief of Cardiology. In the event that any unanticipated adverse events occur, these will be reviewed by the entire study team and reported to the Partners IRB for consideration.
Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners’ IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners’ IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting.

In the unlikely event of an adverse event that occurs during the study, a detailed written report of this event will be completed by the involved study investigator. Each such report will be reviewed by the principal investigator and reported to the Partners IRB.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

All data sheets (surveys and echo classification results) will be reviewed by the principal investigator and at least one other study co-investigator monthly. The principal investigator (Dr. Rory B. Weiner) and Dr David M. Dudzinski will be responsible for ensuring that all data collection forms and acquired study data are complete.

For guidance, refer to the following Partners policies:
Data and Safety Monitoring Plans and Quality Assurance
http://healthcare.partners.org/phsirb/datasafe.htm

Adverse Event Reporting Guidelines
http://healthcare.partners.org/phsirb/adverse_events.htm
### PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

**NOTE:** Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

All study physicians will be assigned a confidential numeric study code. All non-aggregated results will be kept confidential, and only non-identifiable, aggregated data will be shared. All collected datasheets will be kept in a securely locked file with Drs. Weiner and Dudzinski in the Massachusetts General Hospital Division of Cardiology departmental offices.

### SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

This is not applicable.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

This is not applicable.

### RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.
This is not applicable.
**Statistical Analysis Plan:**

**Educational Intervention Reduced the Rate of “Rarely Appropriate” Outpatient Echocardiograms Ordered by Attending Cardiologists: A Randomized Controlled Trial**

Clinicaltrials.gov identifier: NCT01968642

Previous retrospective data from Massachusetts General Hospital suggested that the baseline rate of rarely appropriate (rA) TTE is 22%. Using logistic regression analysis from the software PASS 12 (NCSS, LLC, Kaysville, Utah, USA), we calculated a total number of TTE of 440, split evenly between intervention and control groups, was required to detect a 10% absolute reduction in rA ordering rate, with 80% power and at significance level of 0.05. Categorical variables for cardiologists will be compared using Fisher’s exact test. The median numbers of TTEs ordered by cardiologists in each group will be compared using the Wilcoxon rank-sum test. We will compare the absolute rates of rA, “may be” appropriate, and appropriate TTEs ordered in the intervention group versus control group using a mixed effects logistic regression that will incorporate cardiologists as random effects, with random intercepts to account for any inter-cardiologist differences in ordering. If there are unclassifiable TTEs, they will be excluded from analyses. Statistical analyses will be carried out using R version 3.2.2 (https://www.r-project.org/). Statistical significance will be indicated by p-value <0.05.