

General Template

Version Date: February 2010

Protocol Title: The MedSeq™ Pilot Project: Integrating Whole Genome

Sequencing into Clinical Medicine

Principal Investigator: Robert C. Green, MD, MPH

Site Principal Investigator:

Description of Subject Population: Physicians (Primary Care Physicians) in the

Partners Healthcare System

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Why is this research study being done?

Whole genome sequencing (WGS), which determines the complete DNA sequence of a sample, will soon be inexpensive, accurate, and available for physicians to utilize in the clinical care of patients. Before this happens, it is important for the medical and scientific community to develop a process for integrating WGS information into the current practice of clinical medicine and to explore how physicians and their patients understand and utilize WGS information in healthcare.

We are asking you to take part in this research study because you are a primary care physician within Partners, you have expressed interest in participating in this study, and you see generally healthy adult patients in Primary Care.

Subject Identification

General Template Version Date: February 2010

Approximately 10 primary care physicians and 100 of their generally healthy adult patients and 10 cardiologists and 100 of their adult patients with HCM will be enrolled in this study. Each physician in this study will be asked to recruit and enroll approximately 10 patients from his or her practice to participate. You and your enrolled patients will participate in this study together. In order to ensure that 200 patients total enroll and complete the follow-up period, we will seek to recruit and enroll 300 patients.

The National Institutes of Health is paying for this study to be done.

How long will I take part in this research study?

It will take you approximately 2 years to complete this research study. You will need to make at least 3 in-person visits with the study staff. Your participation in this study includes recruiting approximately 10 patients from your practice to enroll in this study, completing an educational module about genetics and genomics at the beginning of the study, participating in two qualitative interviews and three brief surveys, and your time preparing for and discussing whole genome sequencing results and/or family history information with each of your enrolled patients.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Step 1: Physician education

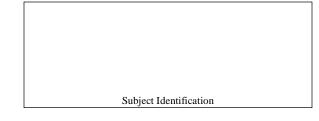
Once 10 primary care physicians and 10 cardiologists are enrolled, the study staff will coordinate a time for you to complete an educational module about genetics and genomics with the other physicians enrolled in this study.

You will be asked to complete a total of 6 hours of education, which includes 2 hours of in-class time with Dr. Murray and 4 hours of online modules. The in-class sessions will be audio and video recorded.

You will be asked to complete a brief survey before and after completing the educational module in order to assess your knowledge of genetics and genomics and your attitudes toward WGS.

You will receive a unique study ID and all survey and interview data will be analyzed using your study ID and not your name or any identifying information.

Step 2: Recruitment of patients from your practice



General Template Version Date: February 2010

You will be responsible for recruiting your own patients into the study. We will ask you to briefly describe the study to eligible patients during routine office visits. If your patient is interested in learning more about the study, you will briefly discuss the study with your patient and ask him or her for permission to forward their contact information to the MedSeq Project staff.

You may also send a recruitment letter and/or call eligible patients directly. Should you approach your patients in this manner, we will ask you to schedule either an in-person appointment or a phone call to review the study with patients who express interest before forwarding your patient's contact information to the study staff.

Once you forward your patient's name to the study staff, we will contact your patient and schedule an appointment for an in-person informed consent meeting. You will not be responsible for consenting patients to take part in this study and you do not need to be present for this informed consent meeting.

Step 3: First qualitative interview

After you complete the educational module and before your first results disclosure visit, you will meet with study personnel for a 45-minute qualitative interview.

Step 4: Receiving your patients' report(s)

Separately, the study staff will randomize each of your patients to either receive WGS or to not receive WGS. If your patient is randomized to receive WGS, you will receive your patient's Genome Report, which includes a General Genome Report, a Cardiac Risk Report, and an Annotated Family History Report. If your patient was randomized to NOT receive WGS, you will receive only the Annotated Family History Report. You will be blinded to your patient's randomization status until the Partners Laboratory for Molecular Medicine sends you the report(s). Your patient will be blinded to his/her randomization status until you disclose the randomization status to him or her at the disclosure visit.

Once you receive your patient's report(s), you will have time to prepare to discuss the results with your patient. You may utilize any resource in preparing for the results disclosure session that you would like, including the MedSeq Project Genetics Resource Center (GRC). The GRC will be staffed with clinical geneticists and genetic counselors to help you understand and interpret the report(s). Should you contact the GRC, the GRC staff will document the consultation to collect data on GRC utilization. This data will be analyzed in aggregate using your study ID and not your name or other identifying information.

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General Template Version Date: February 2010

Step 5: Results disclosure

The study staff will keep track of all of the MedSeq patient visits and when each patient's report(s) have been sent to you. Once you feel adequately prepared for the results disclosure session with your patient, you will be responsible for alerting the study staff. If you have not alerted the study staff that you are prepared to disclose the results within one week of receiving them, the study staff will check in with you periodically. Once you are prepared for the results disclosure, the study staff will work with you and your patient to schedule a time for you to meet with your patient for the results disclosure session.

When you meet with your patient, you will review your patient's report(s) with him or her in whatever depth or detail you feel is appropriate.

You may choose to conduct the results disclosure visit in your clinic, your office or the BWH Center for Clinical Investigation. We will ask you to audio-record the results disclosure visit on recorders that we will provide to you. The study staff will collect your audio-recordings and they will be de-identified, electronically stored on Ms. Lautenbach's computer, and shared with study investigators at Baylor College of Medicine and Duke University.

Study staff will coordinate with you so that they may meet with your patient immediately after the results disclosure session to administer a results disclosure survey in person at the BWH Clinical Center for Investigation.

Step 6: Post-disclosure checklist

Approximately one to two weeks after the results disclosure with a patient, we will ask you to complete a one-page post-disclosure visit checklist, which will take approximately 10 minutes to complete. This brief survey will ask you questions about what actions you considered or took as a result of receiving your patient's Genome Report and/or Family History Report.

Step 7: Medical Record

We will ask you to place your patient's MedSeq Project reports in your patient's medical record and document anything relevant to your patient's care as a result of this study in your patient's medical record.

Step 8: Second Qualitative Interview

Once all of your enrolled patients have completed their 6-month follow-up, the study staff will contact you to schedule an in-person 45-minute qualitative interview. After this interview, your participation in this study will be complete.

Subject Identification

General Template Version Date: February 2010

Storage of your patients' data

Your patients' WGS data and any reports generated from that data will be stored at the Partners Laboratory for Molecular Medicine (LMM). The raw data will be stored for at least the duration of the MedSeq Project grant but no less than 2 years, while recordings will be stored for 10 years and the patients' Genome Reports will be stored indefinitely. For patients randomized to receive WGS as a part of this study, their Genome Reports and Annotated Family History Reports will also be stored at the BWH Adult Genetics Clinic/Personal Genomic Consultation Service. You will be alerted if there are any updates to a patient's report through the existing BWH Adult Genetics Clinic/Personal Genomic Consultation Service Infrastructure.

Review of your patients' medical record

We will review your patients' medical record after all the patients' 6-month follow-up visits are complete. We will collect data regarding tests, procedures, referrals, etc. that have been initiated post-results disclosure. To conduct this medical record review, we will utilize the Partners Patient Data Registry (RPDR) as well as manual chart reviews.

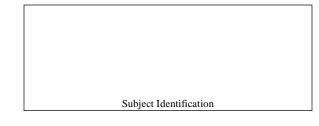
What are the risks and possible discomforts from being in this research study?

There are no anticipated risks to you associated with your participation in this study. You are being asked to operate within the routine practice of medicine and adhere to professional standards. The genomic information about your patients derived as part of this study is an additional informational resource that may or may not be useful in the care of your patients; physicians are professionally expected to integrate a variety of informational sources into their practice and this genomic information is no different.

You may feel uncomfortable with genomic information about your patients derived from this study. The training offered in the Physician Education Module and the Genetics Resource Center Staff is available to support you.

You may also directly contact the PI, Dr. Robert C. Green, at (617) 264-5834, regreen@genetics.med.harvard.edu or the Co-chairs of the MedSeq Project Monitoring Committee, Dr. Judy Garber at (617) 632-2282, Judy Garber@dfci.harvard.edu and Dr. Cynthia Morton at (617) 525-4532, cmorton@partners.com, with any concerns, discomforts or issues that you experience during your participation in the MedSeq Project.

What are the possible benefits from being in this research study?



General Template Version Date: February 2010

There may be no direct benefits to you as a result of participating in this study. You may, however, learn more about genetics, genomics and WGS as a result of participating in this study.

There are several potential benefits to society. Results from this study will provide critical insight into how genomic information may be incorporated into the current practice of clinical medicine and identify areas of further study in subsequent larger randomized controlled trials examining the impact of delivering WGS information to physicians and their patients. There are concerns that information derived from WGS could lead to undesirable outcomes, such as an overutilization of medical resources, vast misunderstanding among physicians and patients, or insurance discrimination. Without actually examining these potential risks within the context of a randomized clinical trial with a physician and patient support system in place, we will not be able to begin to understand the potential benefits, limitations and risks associated with the use of this technology in a clinical setting.

SOME OF THE FOLLOWING LANGUAGE BELOW IS INCLUDED AS STANDARD LANGUAGE TO PROTECT RESEARCH PARTICIPANTS AND THEIR RIGHTS TO RECEIVE MEDICAL CARE AT PARTNERS. HOWEVER, WE WILL NOT COLLECT YOUR HEALTH INFORMATION AS PART OF THIS STUDY, AND THEREFORE, THIS LANGUAGE MAY OR MAY NOT BE APPLICABLE TO YOU AS A PARTICIPATING PHYSICIAN.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

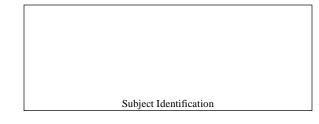
Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

IRB Expiration Date: 6/18/2015



General Template Version Date: February 2010

It is possible that we will have to ask you to drop out before you finish the study. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

You will receive a \$6,000 honorarium for your participation in this study.

What will I have to pay for if I take part in this research study?

You will not have to pay anything to take part in this research study.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

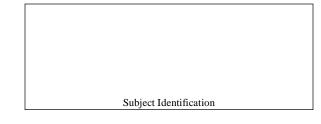
Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Robert C. Green, MD, MPH is the person in charge of this research study. You can call him at $(617)\ 264 - 5834\ Monday - Friday\ 9:00\ AM - 5:00\ PM$. You can also call Denise Lautenbach,



General Template Version Date: February 2010

study.

MS at (617) 264 – 5837 Monday - Friday 9:00 AM – 5:00 PM with questions about this research

If you have questions about the scheduling of appointments or study visits, call Rachel Miller at (617) 264-5885 or Denise Lautenbach, MS at (617) 264 – 5837 Monday – Friday 9:00 AM – 5:00 PM.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 617-424-4100.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

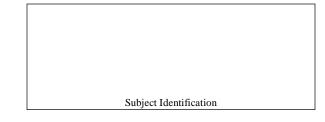
During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research



General Template Version Date: February 2010

- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other: .

Some people or groups who get your health information might not have to follow the same privacy rules that we follow. We share your health information only when we must, and we ask anyone who receives it from us to protect your privacy. However, once your information is shared outside Partners, we cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

IRB Expiration Date: 6/18/2015

Partners HealthCare System Research Consent Form			
General Template Version Date: February 2010	Subject Identification		
You have the right to see and get a copy of your heat treatment or for payment. To ask for this information research study. You may only get such information	n, please contact the person in charge of this		
Informed Consent and Authorization	1		
Statement of Study Doctor or Person Obtaining O	Consent		
 I have explained the research to the study sul I have answered all questions about this research 			
Study Doctor or Person Obtaining Consent	Date/Time		
Statement of Person Giving Informed Consent ar	nd Authorization		
 I have read this consent form. This research study has been explained to me any), other possible treatments or procedures. I have had the opportunity to ask questions. I understand the information given to me. 			
Signature of Subject:			
I give my consent to take part in this research study be used and shared as described above.	and agree to allow my health information to		
Subject	Date/Time		

Page 10 of 10

Consent Form Version: July 18, 2013