

Appendix K

Acceptability of DNA versus Blood Marker Testing

1. Objectives

The HEIRS Acceptability substudy was developed to describe whether, and to what extent, patients have a preference for mode of primary care based screening for iron overload. Two basic modes of hemochromatosis screening are available: a traditional laboratory test that measures iron saturation in the blood (transferrin saturation), and DNA extraction with genotyping for known HFE gene variants and other variants related to iron overload, hemochromatosis, and iron metabolism. While both diagnostic methods are relatively inexpensive, issues of public acceptability of screening have not been assessed. Thus, the primary aim of this study is to compare the acceptability of phenotypic vs. genotypic screening. A secondary aim is to explore potential differences in acceptability of screening method by racial/ethnic group and gender.

1.2 Outcomes

The primary outcome for all study aims will be whether or not (yes/no) the patient expresses willingness to receive hemochromatosis screening. We will compare and contrast the proportion of patients who agree to DNA genotyping to those who agree to the phenotype test.

The secondary outcome will be the mean score of the subjective ratings indicating positive or negative attitudes toward either DNA genotyping or phenotype testing for hemochromatosis.

1.3 Design and Methods

The study is a two 2x2 factorial design (see figure below) involving approximately N=538 per factor, for a total of 1,076 patients per table. The factors are: 1) mode of hemochromatosis screening test (genotype versus phenotype screens), and 2) race/ethnicity (African American/Caucasian). The primary 2 x 2 factorial involves patients recruited at UAB (African American = 528 and Caucasian= 528). An identical 2 x 2 factorial of 1,076 patients is planned based on sites with high proportions of African American and Caucasian patients recruited from sites not in the southeastern region of the U.S.

Procedures

1. Overview.

Substudy-1 will occur in three HEIRS centers, with a goal of recruiting and randomizing approximately 2,152 patients (African Americans and Caucasians) to two conditions: initial description of either a phenotype or genotype HH testing. In each condition, patients will read information about the phenotype test that describes how the test will be taken, some general implications regarding the interpretation a positive or negative result, and logistic information such as need for repeat visits. After completing a brief survey about their attitudes about iron overload screening, patients will be invited to complete an HEIRS informed consent where they will receive the full and complete description of HEIRS. It is at this point that the substudy assessment procedures end, and the formal HEIRS recruitment and screening procedures begin without interruption. The process is expected to take approximately 5 minutes to complete.

1.2. Preparation

Forms

Have at hand, several unopened sequentially numbered questionnaire packets including either:

- 1) A one page document "Patient Information about Hemochromatosis and Iron Overload (group 1), attached to each a blue and yellow paper color survey form; one (1) 8.5" x 11' manila envelope*
- 2) A one page document "Patient Information about Hemochromatosis and Iron Overload (group 2), attached to each a pink and green paper color survey form; one (1) 8.5" x 11' manila envelope*

Each form and envelope will be pre-labeled with a 9 digit study ID number (4 digits) and sequence number (4 digits), and location number (1 digit). This number will be used only by the substudy, and will not be recorded on HEIRS forms.

Other Supplies

Have ready a sufficient number of the Study Disposition Form.

Have a sufficient supply of pencils or pens, and clipboards, for patient use to complete the study forms.

Recruitment

Substudy recruitment will occur during the HEIRS Initial Screening Visit during, beginning August 2001.

Recruitment.

After completing the HEIRS age screen and ascertaining that the patient is age 25 years or older, the following steps should be taken for age-eligibles:

- 1) Invite the person to read a brief one-page description about hemochromatosis screening which includes completing a brief (one-page) survey. You should be familiar with all of the materials included in the packet so as to answer any questions that might arise prior to the patient assenting to participate in the substudy. (*note: we don't know if some sites will require a special consent form.*) It is important to realize that at this point the patient is not being asked to participate in HEIRS. He/she is only being asked to read a brief description and answer a questions about willingness to have an HH screen.
- 2) Tell the patient that their responses are confidential and that their name will not be recorded on the study form, or elsewhere.
- 3) Be aware that this substudy is not attempting to determine whether or not a patient would like to participate in HEIRS, but is assessing their attitudes and opinions about iron overload or genetic screening. After completing the substudy survey, the patient will receive the standard HEIRS Initial Screening Visit protocol.

Distributing the forms

Substudy participants are those who agree to read the HH description and complete the form. When the patient has agreed to participate complete the following steps:

- 1) Patients will be assigned to groups by numerical ordering of the sealed packets according to a four digit envelope number printed on the upper left hand corner. Open the envelope and hand the survey to the participant, along with a pencil or pen suitable marking the forms, and clipboard .
- 2) Tell the participant to carefully read the first page, following the instructions on the bottom of the page that say which one survey of the two color-coded surveys enclosed he/she will need to complete. Show the participant a sample page 1 form:

“you will see a page similar to this”. Point to the instructions on the page that tell how to select the survey to complete: “after you read this paragraph about iron overload screening, the instructions on the bottom of this page will tell you which survey to complete”.

- 3) Instruct the participant to answer each question on the form.
- 4) Tell the participant to place all of the materials in the enclosed envelope once the survey has been completed. This envelope has the same number in the upper left-hand corner as the original outside envelope that contained the study packet.

The Setting

- 1) In order to answer questions that may arise, the data collector should be readily accessible to the respondent while the questionnaire is being completed. The questionnaire should be completed in one sitting in the clinic location.
- 2) The recruiter should select a clinic location that provides adequate privacy and confidentiality to the participant, for example, a context where the participant may complete the survey without drawing attention of other persons in the waiting area.
- 3) If conducted in a clinic environment, the participant must be able to read and complete the study packet without the presence of a healthcare provider, and in a context in which it is clear that the completing the survey is not a part of the participants health care process.

Assisting the Participant

- 1) Questions asked by the participant about how to complete or return the information may be answered factually, as appropriate. It is important that questions asked about HH screening must be answered in a way which does not add additional detail to what has been provided in brief description. As a general guide, aspects of the brief HH description that are not understood may be clarified only using words and terms already provided and in a way which does not expand or provide additional information. For example, if asked to clarify what is meant by “organ damage” a response of “liver damage and heart disease are some examples.”
- 2) Some of the participants might have questions about items on the survey. In answering questions, survey administrators must be careful not to bias the participants' responses. The data collector may read a question to a respondent, define terms, indicate where the answer is to be marked, etc., but they should not paraphrase questions unless it is absolutely necessary. It is easy to alter the meaning of a question

in this way. Therefore, the data collector should not suggest an answer for the participant. In general, most of the participant's questions can be handled by reminding him/her to follow the directions on the questionnaire, or simply by rereading the statement to the respondent. The interviewer should read the statement exactly as it is written. The interviewer may indicate to the participant that there are no right or wrong answers to the questions, and that the choice is his/hers as to how to respond to the statement. Under no circumstances should the survey administrator help the participant decide how to mark a questionnaire item.

3) The survey questions ask primarily about willingness to be screened and are to be completed by the participant (i.e., self-administered). Although it is not anticipated to be frequent, special situations will arise in which factors such as poor eyesight, poor hand-eye coordination, ill health, and language or reading skill levels may preclude a participant from completing the forms. It is permissible for patients to have a friend or family member assist them in reading the study material. Because an aim of this study is to record the patients viewpoint and attitudes about HH screening without potential, unintended, influence from the HEIRS staff, it is not permissible to read the form to the participant.

Competency

If you believe the participant is having difficulty completing the survey because of competency you should explain, in a way that will not cause offense, that they do not need to continue. It may be difficult to recognize participants with low literacy skills unless the participant verbalizes that he/she is unable to read at a level sufficient to complete the questionnaire. Cues to low reading skills may include the participant asking many questions, completing the measures very slowly, glancing up and around, appearing confused, or checking off responses without clearly reading the items).

Non-English languages. Patients recruited in the substudy are required to read and speak English. However, it is permissible for non-English-speaking patients to rely on a friend or family member as translator in reading and understanding the consent form.

Handling the Completed Forms

- 1) Make sure that the participant has placed the study material in the enclosed manila envelope.
- 2) Every envelope must be accounted for on the Study Disposition Form. If an envelope is lost or not returned it is necessary to fill-in the comment area on the Form, describing the reason for non-return.

Transitioning to the HEIRS Informed Consent Procedures

- 1) Thank the participant for completing the forms.
- 2) Once the substudy packet has been returned to the study staff person, the HEIRS recruitment flow should proceed according to protocol (*note: need to review the Recruitment Chapter to refine this transition as needed.*)
- 3) The substudy forms should be kept in the returned envelope, and should not be used as a basis to determine interest in conducting an informed consent or discussed with the patient.

Completing the Substudy Disposition Form

- 1) After the informed consent process has been completed, indicate on the form the final disposition (enrolled/ not enrolled).

Storing and Forwarding the Completed Substudy Forms

Once a questionnaire has been completed by a participant and edited by the survey administrator, the questionnaire should be stored in a secure place within the clinic. The questionnaire should not be left unattended where non-research staff can review the participants' responses. Information collected for research purposes can only be shared with other members of the research team, and the participants' privacy must be protected at all times.

