Manual of Procedures (MOP)
Section 6. Screening

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6.1 OVERVIEW

At most sites, the screening and informed consent process are staged into 2 parts, a *Pre-screening* phase followed by a formal *Screening* visit. Each site, based on its prior experience, has developed a detailed site-specific recruitment plan (based on MOP section 5) that includes a pre-screening recruitment strategy to identify individuals at increased risk for type 2 diabetes who will be invited to the in-person screening visit. Active recruitment will take place year round at regular rates of enrollment to ensure equal exposure of randomized participants to UV-B.

6.2 PRE-SCREENING

The goals of the pre-screening phase are to: 1) identify potentially eligible participants; 2) initiate the informed consent process; 3) conduct a preliminary verification of eligibility; 4) promote efficiency by pre-selecting candidates with high likelihood of eligibility after screening; 5) allow sites flexibility in their approach of recruiting participants, while maintaining a study-specific set of inclusion/exclusion criteria.

The target for the screening process is to have a screened-to-randomization ratio close to 3:1 or better.

The pre-screening phase is site-specific and is based on what has worked well previously at the site. Pre-screening takes place in one, two, or more stages that may include an additional visit (e.g. identification of potential participants through databases [pre-screening stage 1], followed by over-the-phone pre-screening [pre-screening stage 2], followed by a visit [pre-screening stage 3].

Sites will employ a variety of sources including electronic databases (e.g. electronic medical records and research volunteer databases), community-based advertising (e.g. hospital newsletters and specific local newspapers), targeted outpatient hospital clinics (e.g. primary care, cardiology), mailings to primary care physicians in each metropolitan area, social media (e.g. Craigslist), and study press releases to local news media to recruit potential participants (see MOP section 5).

6.2.1 Pre-Screening Procedures

The following are examples of pre-screening approaches that sites may follow.

6.2.1.1 Over the Phone

When a person calls to inquire about D2d, first impressions are important. Introduce yourself and explain your role in the study (Research Coordinator, Recruitment Coordinator, etc.) to the caller. Phone inquiries about the study are a great way to assess the effectiveness of the site-specific recruitment strategies, so it is important to ask interested volunteers where and how they heard about the study or what prompted them to call.

The research staff reads a simple script (see Appendix) to callers providing a brief overview of the study, informing them that they will be asked questions to determine preliminary eligibility and that, if eligible, they will be invited to the research site for an in-person screening visit. The caller will then be

asked if she would like to continue with the call and if she agrees; the research staff will continue with the Pre-screening Questionnaire that evaluates the key inclusion/exclusion criteria (see Appendix).

If the volunteer appears to qualify after the pre-screening questionnaire, a diabetes risk score may be administered next as a second level of pre-screening. One such example is the American Diabetes Association Diabetes Risk Test, which is available on-line (http://www.diabetes.org/diabetes-basics/prevention/diabetes-risk-test) and in the Appendix.

A site may also have a pre-screening questionnaire available on its page on the study's website for interested volunteers to complete (see http://www.d2dstudy.org/tufts-medical-center-site-page-2).

6.2.1.2 In Person

Pre-screening may also be conducted in person in a number of settings or events, as described below. In these settings or events, people will be provided information about the study (e.g. study brochures) and pre-screening activities may be completed. Regardless of where the in-person pre-screening takes place, ensuring privacy is essential.

Examples of settings for in-person screening include:

- Waiting rooms in outpatient clinics while patients wait for their appointments.
- Public events where a table can be set-up
    - Recreational events [farmers markets, sports, racing, festivals]
    - Health fairs
    - Community gathering places [bingo, flea markets]
- Medical center cafeterias

Sites may consider conducting a simple pre-screening visit (e.g. vital signs, point-of-care glucose testing) that may be used to pre-screen for D2d but also as an opportunity to gather information for people who are interested in participating in research to enter in a participant research database.

6.2.1.3 Database Review

Querying databases to identify potentially eligible volunteers is an efficient and potentially cost-effective recruitment strategy. Below are examples of databases that may be available at the sites. Please refer to MOP section 5 for additional details.

- Electronic Medical Record systems
- Research Participant Databases/Registries

6.3 SCREENING VISIT

If the interested volunteer has met all inclusion and no exclusion criteria during the pre-screening (preferably, also including meeting some indication of being at increased risk for diabetes), he will be invited in for a screening visit, which will be identical at all sites.

If the potential participant wants to read (or if it would be helpful for him to read) the informed consent forms prior to the screening visit, the forms can be sent to him. A site may also make consent forms available on its page on the study's website for interested volunteers to review.

⇒ ***It is important to inform the potential participant that he should come to the screening visit after fasting for 8 hours, to bring all medications and supplements with him, and to not participate in vigorous physical activity for 24 hours before the visit.***

6.3.1 Informed Consent Process

At first contact with participants, prior to any study specific procedures, the informed consent process will be started. If the first contact is over the phone (see pre-screening above), a sample script (see Appendix) will be read to the potential participant providing a brief overview of the study, informing her that she will be asked questions to determine if she is potentially eligible, and, if she is potentially eligible, she will be invited to the research site for a screening visit.

At the first (screening) visit, written informed consent for the main study will be obtained prior to any study procedures.

Then, the informed consent process for the D2d Research Repository should be initiated. The informed consent process for the Specimen Repository should be conducted following the same guidelines as the consent for the study.

The informed consent process is ongoing and interactive. Participants will be given the opportunity to ask questions throughout their participation in the study. Participants will be told that they can cease participating in the study at any time for any reason.

6.3.1.1 Setting

The consent process should be conducted in a comfortable relaxed setting by the site PI or other qualified member of the site research team (e.g. co-investigator, research coordinator, research assistant, or clinical research nurse) with in-depth knowledge of D2d, as delegated by the site PI.

6.3.1.2 Content

The full nature of the study (purpose, procedures, risks, potential benefits, etc.) will be reviewed in detail.

⇒ *The importance of the study and the need to return for all scheduled visits and follow all study procedures even if the study pills have been stopped will be emphasized.*

Volunteers will be informed that they can cease participating in the study at any time for any reason.

6.3.1.3 Discussion

The person responsible for obtaining consent should encourage questions and a discussion. The process must not be rushed. Volunteers must be given ample time to review the ICFs.

6.3.1.4 Assessment of Comprehension

The volunteer should demonstrate an understanding of the study prior to being asked to sign the ICFs. For example, staff may ask the volunteer questions or the volunteer may verbalize what will happen or asking relevant detailed questions.

6.3.1.5 Documentation of Informed Consent

Once all questions have been answered and concerns addressed, the volunteer participant will be asked to sign the written informed consent form for the main study. The Informed Consent Form (ICF) must be signed in the presence of the site PI (or designee). The original must be saved in the participant's folder and a copy of the signed form will be provided to the participant.

As documentation of the informed consent process, the following should be included in the source document: who led the discussion, who was present during the discussion, any issues (including any notable concerns or questions raised by the participant), and the date and time when written informed consent was obtained.

Documentation of informed consent is also recorded in the EDC system.

6.4 SCREENING ACTIVITIES

After written informed consent has been obtained, screening should proceed as follows:

Note: If at any point during the screening visit, it is determined that the participant meets an exclusion criterion, the remaining activities do not need to be completed.

6.4.1 Basic demographic information (if not done previously)

- ✓ Date of birth, race and ethnicity

6.4.2 Physical Measurements (vital signs)

- ✓ Measure blood pressure and heart rate, following procedures in MOP section 11. Blood pressure and heart rate are done first, as other measures (e.g. weight) can be stressful and can impact blood pressure and heart rate.
- ✓ Measure height and weight, following procedures in MOP section 11.
- ✓ Calculate BMI.
    - This may be done by entering the height and weight in EDC (see MOP section 15)
    - An online BMI calculator, such as the one provided by the NIH, can be used to calculate BMI (http://www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm), choose the metric tab, and enter in the height and weight measured.
    - A hard copy of a BMI chart can be utilized (see Appendix). If the participant weight/height falls on the border of eligibility, it is recommended that a BMI calculator be used to accurately calculate the BMI to the first decimal point.

6.4.3 Medical history

- ✓ Obtain complete medical history. This task must be completed by staff trained to take medical history (e.g. physician investigator, nurse).
- ✓ The participant should be asked if she has or had any medical problems related to each system, with emphasis on conditions relevant to the inclusion/exclusion criteria (e.g. have you ever had a kidney stone?).

6.4.4 Review of concomitant medications and supplements

- ✓ If the participant came to the visit with her medications and supplements, go over all prescribed medications, over the counter medications and supplements, recording the dosage, frequency, the reason for taking the medication, and start date (approximate is okay). If the participant did not bring the actual medications but came with a list, review the list with the participant and collect as much detail as possible.

- ✓ If the participant reports taking a medication that is not for the treatment of any condition reported during the medical history, seek clarification from the participant.

- ✓ Staff, in consultation with the site PI, should review the participants' concomitant medication and supplement list to ensure that the participant is not taking any excluded medications (see MOP section 8).

- ✓ The research coordinator must add up the total dosage of non-dietary vitamin D a participant is taking to make sure the total daily dose does not exceed 1000 IU/day. For example, 800 IU/day in a multivitamin and 2800 IU/week [=400 IU/day] from Fosamax Plus D = 1200 IU/day, which excludes volunteer.

- ✓ The research coordinator must add up the total dosage of non-dietary calcium a participant is taking to make sure the total daily dose does not exceed 600 mg/day.

⇒ *Special attention should be made to ensure that the participant understands the calcium and vitamin D supplements restrictions and the rationale behind the restrictions*.

- ✓ Remind the participant to call the Research Coordinator or designee to discuss any changes in medications between study visits.

- ✓ Please note that although all medications and supplement use will be recorded in source documents, only certain medications and supplements will be entered in the EDC (see MOP section 8.5.2).

6.4.5 Laboratory Specimen Collection

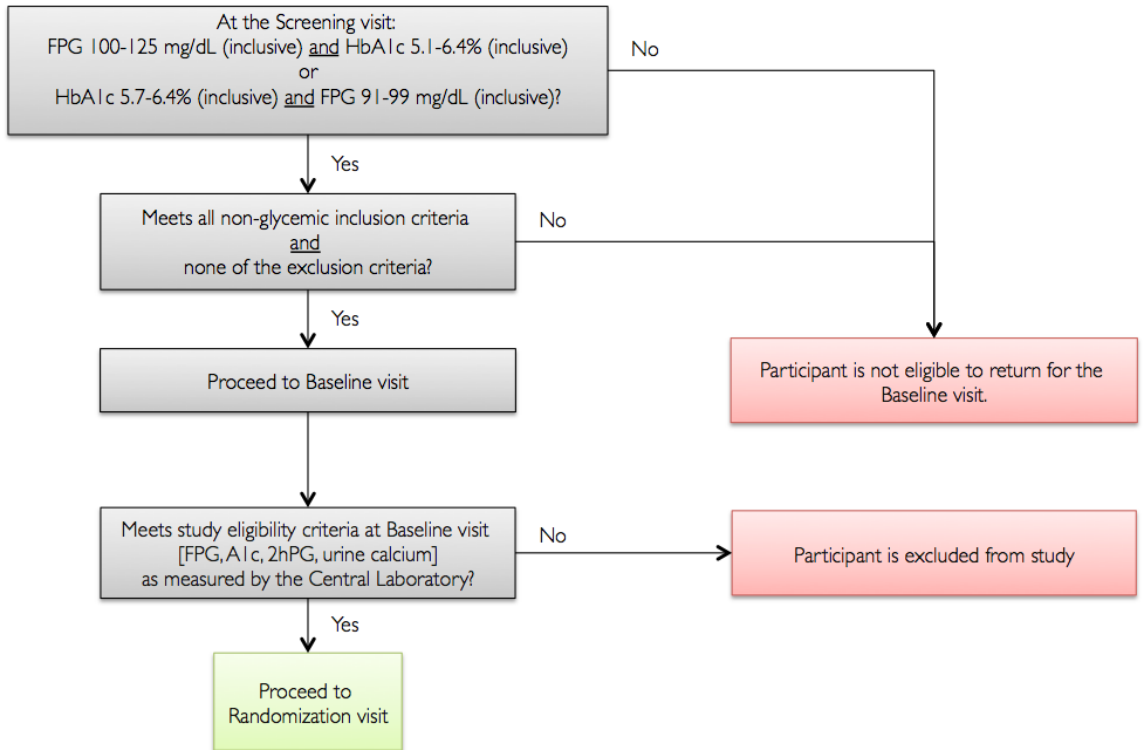
- ✓ Blood and urine will be collected, while participant is fasting, and analyzed at the local site laboratory. Please see MOP section 9 for detailed instructions.

- ✓ Provide the participant with food and drink.

- ✓ Review assessment of eligibility based on safety laboratory criteria.

- ✓ Assessment of further eligibility based on glycemic criteria is shown in Figure 6.1 (same as Protocol Figure 6.1)

Figure 6.1: Flow diagram of assessment of eligibility at screening and baseline visits



6.4.6 Administrative Activities

If it appears from the history and physical measures, that the participant may be eligible to return for the baseline visit, please obtain the following information:

6.4.6.1 Contact Information

Participants will state their preferred method of communication (email, phone, text etc.) with the research staff. If e-mail is agreed upon as the preferred method of communication, participants should be instructed to respond to emails, thereby letting the research staff sender know the message was received. It is best to obtain a few different ways to reach the participant. Please see source document titled Participant Contact Information, in MOP section 13.

6.4.6.2 Medical Release

- ✓ Offer to share the participant's laboratory results with her primary care provider (PCP).
- ✓ Explain that D2d procedures require that the PCP provides results of laboratory tests done in the PCP's office to the researchers as needed.
- ✓ If the participant is amenable, have the participant sign a medical release authorizing you to share information with the PCP and authorizing the PCP to share information with the research staff.
- ✓ There is no template form provided by D2d. Please use a site-specific medical release form.

6.4.7 Establish a follow-up plan with the participant

The site can either:

a. Make a tentative baseline appointment for the participant and confirm the date once the glycemia and safety laboratory results have been reviewed.

b. Set up a time to call the participant and report the results and if participant qualifies, schedule the baseline appointment.

6.4.8 Screening failures

If during the screening visit, it is determined a participant meets an exclusion criterion, his participation will end and no other screening activities need to be completed. The participant should be provided with a snack and drink and thanked for his time and effort.

If, after reviewing the screening laboratory results, the participant does not qualify to return for the baseline visit, she should be notified by her preferred method of communication (e.g. phone, email).

Note regarding repeat screening: If the exclusion criterion was one that is modifiable or may resolve (e.g. elevated blood pressure, recent initiation of oral contraceptives), the participant should be informed to contact the site in the future for re-screening. The site should also note the circumstances and plan on re-contacting the participant if appropriate.

- ✓ *A participant may be re-screened up to an additional 2 times.*

- ✓ A personal thank you note signed by the staff who met with the participant should be sent a few days after the visit, thanking the person for her willingness to come to a screening visit. Personal thank you notes are often a pleasant surprise and an appreciated gesture, which may lead to future willingness to participate in research, or may lead to referrals from friends or relatives who may also be at risk for diabetes.

6.4.8.1 Diabetes diagnosed at screening visit

Given their high-risk profile, it is expected that some individuals will be found to have previously unrecognized hyperglycemia in the diabetes range (i.e. HbA1c ≥ 6.5%, FPG ≥ 126 mg/dL and/or 2hPG ≥ 200 mg/dL). These people are ineligible to participate in D2d and they will receive an informational letter (MOP section 20) indicating the possibility that they may have diabetes and should be seen by their primary care provider to confirm the diagnosis of diabetes and to initiate appropriate therapy. Participants will be mailed copies of their laboratory results to share with their primary care provider, but study personnel will not participate in any further evaluation or treatment of participants who are found to have diabetes at screening.

6.5 APPENDICES

Appendix 1 **Pre-screening Template Introductory Phone Script**

Appendix 2 **Pre-screening Template Inclusion Exclusion Criteria Questionnaire (includes BMI Table)**

Appendix 3 **American Diabetes Association Diabetes Risk Test**