Section 1
Women's Health Initiative (WHI) Extension Study Protocol
December 7, 2011

Sub-Section describing the In-person Visit

5.4 In-person Visit

A target sample size of 8,000 women aged 72 or more will participate in the in-person visit (WHI Long Life Study), scheduled to begin in late 2011. To complete data collection on 8,000 women, an eligible population of approximately 10,000 women will be selected for inclusion as follows: All WHI Memory Study (WHIMS) participants and non-WHIMS MRC participants who will be at least age 72 by 12/1/2011. All eligible participants will have both genome wide study data (GWAS) and baseline biomarker data (glucose, insulin, CRP, creatinine, triglycerides, total cholesterol, LDL, and HDL) available. Participants will be excluded if they reside in an institution (e.g., skilled nursing facility).

The data and blood collected in this study will establish a new baseline from which numerous studies on aging and health/disease can be conducted. A brief clinical assessment will be conducted on all participants, including an assessment of functional status. The primary aims of the blood collection are to (1) establish a repository of new baseline biospecimen on this cohort, (2) replenish the WHI biospecimen resource for members of this cohort with a new source of good quality extracted DNA and RNA, plasma, serum, and RBCs for future standard clinical laboratory assays as well as cytokines, proteomics, metabolomics, and other assays that have yet to be imagined, and (3) obtain CBC data (e.g., hemoglobin, white blood cell count) and CVD biomarker data (glucose, insulin, creatinine, CRP, total cholesterol, HDL, LDL, and triglycerides).

A closely related ancillary study, Objective Physical Activity and Cardiovascular Health in Women Aged 80 and Older (OPACH80, PI Andrea LaCroix), has been funded. The goals of this study are similar to the in-person visit in that the objective is to increase understanding of the health of aging women – specifically the association of physical activity with cardiovascular events and total mortality. OPACH80 was designed to collect most of its data as part of the in-person visit. This protocol treats OPACH80 as part of the In-person Visit. The eligible population for OPACH80 will be identical to the In-person Visit with one exception: OPACH80 will exclude women who are non-ambulatory.

Another ancillary study, Evidence for Establishing Optimum Protein Intake in Older Adults (WHI-Food Intake Study, AS340, PI Jeannette Beasley), will begin immediately following the In-person Visit and has the identical eligible population. The In-person Visit post-visit thank you letter packet will introduce participants to AS 340 and provide a Food Frequency Questionnaire (FFQ). (The AS340 cover letter and FFQ, and Waiver of documentation of consent for the AS340 FFQ, were IRB approved as part of the WHI Extension on 9/23/11).

Consent: Over a 12 month period, the CCC will send an In-person Visit consent mailing to the selected women. The initial consent mailing will be preceded by an Advance Postcard designed to pique the interest of eligible women. The consent packet will include a letter explaining the nature and purpose of the study, two copies of a consent form and a self-addressed, postage pre-paid envelope. The women will be given a toll-free number to call with questions and asked to sign the consent and return the signature page from one copy of it to the CCC in the envelope provided. One week after the initial consent mailing, all women will receive a thank you/reminder post card. Women who have not responded within three weeks of the initial mailing will be sent a second consent packet. Finally, women who have not responded within 6 weeks of the initial consent mailing will be called by interviewers from FHCRC-based staff - (Collaborative Data Services (CDS) or CCC staff) for either telephone consent or a reminder to return their consent form. Typically, the CDS staff will make at least 3 attempts to contact non-responders to obtain telephone consent. A similar consent process was successfully implemented for the WHI Extension II consent. However, for the in-person visit telephone consent will be confirmed at the outset of the in-person visit and documented by the woman's signature on a consent form.

Scheduling: Once the CCC has received documentation of IPV consent for a woman (signed copy of the consent form or telephone consent form signed by the interviewer who obtained telephone consent), the CCC will notify the organization subcontracted for the data collection (Examination Management Services, Inc. – EMSI), providing them with the participant's name, address, telephone number and study ID. The EMSI staff will contact the participant to arrange a mutually agreeable date, time and location for an in-person data collection visit. The visit may occur in the participant's own home or, if she prefers, her physician's office or a facility operated by EMSI.

Training/Certification: In concert with EMSI's project coordinator, the CCC will develop, test (alpha and beta), revise if needed, and implement a centralized Web-based training program for all EMSI examiners (also referred to in this protocol as research assistants - RAs) who might be assigned to WHI participants. The Web-based training program will culminate in a test, with feedback provided for every incorrect answer and ≥ 90% correct answers required for certification. If initial testing results in <90% correct answers, repeating the training course a week later will be required. If more than one month has passed between a RA's certification and assignment to a WHI case, re-certification will be required. If less than one month has passed between an RA's certification and assignment to a WHI case, review of the training course will be highly encouraged.

Data Collection: In addition to the project-specific training, EMSI will ensure that each RA scheduled to collect data from a WHI participant is trained/certified on protection of human subjects in research, trained/certified in phlebotomy, passed a felony record search and drug screen, completed a customer service training program, and completed/passed a HIPAA training program. The EMSI Scheduling staff will have a separate training/certification program developed by the CCC – as will the FHCRC-based staff who will conduct the telephone consent calls.

The in-person visit will require about 70 minutes and include:

- Physical measurements: height, weight, blood pressure, pulse, waist circumference
- Blood draw (~ 31ml)
- Physical function measurements: balance, gait speed, chair stand, grip strength
- OPACH80 adds the following to the in-person visit (among ambulatory participants):
    - Delivery of a self-explanatory survey packet
        - physical activity questionnaire
        - a monthly falls/injuries reporting system (via postcard)
    - Delivery of a self-explanatory physical activity monitor packet and brief instruction on use of the monitor by participants for seven days following the in-person appointment

Blood Processing: Immediately after the in-person visit, the RA will travel to an appropriate location to prepare the blood vials within two hours of draw for overnight shipment to the central lab (FHCRC Specimen Processing Lab). Upon receipt of each in-person visit shipment, the central lab will open the package and assess the contents for completeness and adequacy of packaging, deliver the CBC vial to the testing lab (Seattle Cancer Care Alliance Hematology Lab), and process the remaining blood vials according to the manual of operations. Blood samples will be frozen and stored for future DNA and RNA extraction (within ~ one month). All other aliquots will be frozen and shipped to the WHI Biorepository. One of the serum aliquots for each participant will be sent from the Biorepository to the University of Minnesota Fairview Lab for biomarker testing (lipids, glucose, insulin, creatinine, and CRP) within approximately 6-12 months of the draw date.

Data Processing: Immediately following the shipment of blood to the central lab, EMSI will fax the completed study forms to EMSI's central office, where they will be stored only as an electronic image. Original hard copy forms will be held securely at the branch office until it receives official notification from WHI that the project is completed, at which time the hard copy forms will be shredded. Daily, EMSI's central office will submit electronic copies of collected data forms to the WHI CCC via FTP. Data will be reviewed and key-entered by WHI CCC staff.

Post-visit Letter: Within about two weeks of the in-person visit, the CCC will send participants a thank you letter. The letter will include the participant's CBC results and advice for discussing the results with their doctor if necessary. (If the CBC results require urgent action, a CCC staff member will call the participant in advance of the letter.) If the participant returns the physical activity monitor as instructed, and should funds be available, the letter will also include $10 as small token of our appreciation. (The mailing and the gift card will be paid for with OPACH80 funds.) As the biomarker assays (lipids, glucose, insulin, creatinine, CRP) will not be completed until ~6-12 months after the blood draw, those results would not be considered clinically relevant – and will not be provided to the participant. The post-visit letter will also include an AS340 cover letter, a FFQ, and a $2 token incentive (should funds be available).

Post- In-person Visit OPACH Calibration Study: Following the in-person visits, OPACH80 will conduct an accelerometer (physical activity monitor) calibration study among 200 participants. The calibration study data will be collected at two WHI clinic sites (Stanford U. and U. of Alabama, Birmingham). Women will be eligible to participate in a clinic visit if they meet the following criteria: (1) residence near either the Stanford or Birmingham clinic, (2) originally recruited into the WHI at either Stanford or Birmingham, (3) wore the physical activity monitor for seven days, (4) able to walk without a walker, (5) lack major mobility disability as determined by a score of ≥ 4 on the Short Physical Performance Battery (SPPB), (6) able to walk at least 400 meters (self-reported), (7) no history of clinically significant CHD (MI or angina), emphysema, asthma, or other condition causing chest pain or shortness of breath during walking, and (8) willing to participate and to provide informed consent. The initial eligibility list will be prepared by the CCC based on WHI database information and the SPPB performed at the in-person visit. The Stanford and Birmingham clinic staff will collect remaining exclusion criteria data during a brief (~10 minute) phone interview. Final decisions on eligibility will be made by the CCC.

Calibration Study Consent: The in-person visit consent form will mention the possibility of a future invitation for a clinic visit. Once selected as eligible for the clinic visit, women will be called by staff at the CCC or her WHI Regional Center, invited to join the clinic phase of the study, and introduced to the clinic visit activities. If interested and willing, a clinic appointment will be set. At the clinic visit, the participant will have time to read the in-person visit consent form and ask questions to the clinic staff. If the participant signs the consent, the clinic visit assessments will continue. Calibration study participants will receive a $25 gift card for participating.

The calibration study clinic visit will take 30 - 90 minutes and include:

- Body height and weight using a calibrated balance-beam scale and a standiometer.
- CHAMPS physical activity questionnaire and WHI Physical Activity Questionnaire (PAQ), which will provide contemporaneous measures of physical activity level and walking performance.
- Rating of perceived exercise capacity using a scale developed by Wisen [Wisen et al, 2002] that explained 66% of the variance in aerobic capacity in women age 20 to 80.
- 400 meter walk, using the protocol of the LIFE-P study that involves walking 10 laps around an indoor course. The test is stopped if participants cannot complete the walk in 15 minutes. Participants may use a cane during the walk, but cannot use a walker or other assistive device.
- Accelerometer and step counts during the 400 meter walk, measured using the Actigraph GT3X during the walk with the step counter function turned on.
- Accelerometer counts/min and oxygen consumption during standardized tasks.

Quality Control: The CCC will monitor the quality, quantity, and timeliness of all in-person visit operations, including the calibration study. The CCC project coordinator will meet via conference call at least monthly with the EMSI project coordinator to review reports (training, scheduling, and visit completion), discuss concerns and successes, and make adjustments as required. Adherence to the in-person visit protocol will be monitored by the CCC via direct site visit observations, review of completed forms, reports from the central lab, and EMSI routine performance reviews.

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