

WOMEN'S INTERAGENCY HIV STUDY

SECTION 33: ASSESSMENT OF PHYSICAL FUNCTIONING

A. STUDY PURPOSE

The overall objective of this assessment is to identify and characterize physical impairment within a cohort of HIV-infected women. The term physical impairment is used broadly to include components of frailty syndrome, mobility-based instrumental activities of daily living (IADLs) tasks, and the physical functioning component of the Quality of Life (QOL) scale. Based on biologic plausibility, we hypothesize that HIV provides sufficient insult to push those with 1) low physiologic reserves, 2) compromised immunity (due to aging or medical history), and/or 3) a predisposition toward frailty into clinically manifesting frailty or other forms of physical impairment.

Evaluation of physical disability in the context of HIV will enable providers and policymakers alike to identify more appropriate and effective health services for HIV-infected persons. Improved care may decrease overall health service burden. Moreover, HIV-infected women will reduce their risk of institutionalization and death, and could experience an extended period of independence, as well as an improved quality of life (Rusch; Stanton).

While our hypothesized causal pathway of HIV with physical impairment places frailty as an intermediate step towards mobility-based IADL disability and decreased physical functioning on the QOL scale, we treat all three as separate outcomes. Because each of these measures quantifies impairment, there is likely to be overlap. Treating all three as separate outcomes will enable us to evaluate whether they identify as impaired the same subgroup of women. If there is high correlation, we know that permanent incorporation of the frailty index or IADL instrument into the WIHS questionnaire (which already contains the QOL scale) will be unnecessary.

B. HYPOTHESES AND SPECIFIC AIMS

The hypotheses below are based on the following theories or observations: 1) women with advanced HIV disease will exhibit greater frailty, increased mobility-based IADL disability, and decreased physical functioning-related QOL compared to those without HIV; 2) being older (> 50 years) with HIV modifies and increases the risk of physical impairment; 3) those with advanced HIV disease will demonstrate greater cognitive impairment than those without advanced disease; and 4) neurocognitive impairment in HIV-infected persons will be associated with the presentation of frailty and other expressions of physical disability as compared to those without impairment.

Aim 1: To characterize the frequency of disability as measured via frailty, mobility-related instrumental activities of daily living (IADL), and physical functioning-related quality of life (QOL) measures among HIV-infected and at-risk HIV-uninfected women.

- Hypothesis 1.1: The prevalence of impairment in IADL tasks will be 15% and 32% for HIV-uninfected and HIV-infected women, respectively.
- Hypothesis 1.2: The prevalence of frailty (presenting at least three out of the five criteria) in HIV-infected women will be approximately 8% and the prevalence of intermediate frailty (presenting at least one out of five) will be 40%.
- Hypothesis 1.3: The QOL physical functioning score for unimpaired HIV-infected women will be 88 out of 100, while impaired HIV-infected women will have a lower score of 80. Higher scores reflect better quality of life.

Aim 2: To compare three instruments of physical impairment (frailty, mobility-based IADL disability, and physical functioning-related QOL) and determine the correlation between instruments across subgroups in the WIHS cohort. The purpose of this aim is to evaluate whether each of the measures (frailty, IADL, and ADL) contribute data different than that obtained in the current WIHS instrument (i.e., F26).

- Hypothesis 2.1: There is a relationship between frailty, mobility-based IADL disability, and physical functioning-related quality of life instruments.
- Hypothesis 2.2: The relationship among frailty, mobility-based IADL disability, and physical functioning-related quality of life instruments varies by age group (younger versus older).
- Hypothesis 2.3: The relationship among frailty, mobility-based IADL disability, and physical functioning-related quality of life instruments varies by HIV status.
- Hypothesis 2.4: There is a difference in frailty, mobility-based IADL disability, and physical functioning-related quality of life instruments in those with and without neurocognitive impairment.

Aim 3: To compare the distribution of physical impairment scores of HIV-infected women with internal, at-risk HIV-uninfected controls, and external, healthy HIV-uninfected controls from the Cardiovascular Health Study (CHS) and the Women’s Health and Aging Study (WHAS). This will enable us to evaluate the “ecological” differences in physical impairment compared to external controls.

- Hypothesis 3.1: There is a difference in the prevalence and severity of physical deficits, as measured by frailty, mobility IADLs, and QOL scores, in HIV-infected women versus at-risk HIV-uninfected women.
- Hypothesis 3.2: Among women with HAART-related side effects, the prevalence and severity of physical deficits in HIV-infected women treated with highly active antiretroviral therapy will remain higher than that of HIV-uninfected women.
- Hypothesis 3.3: The prevalence and severity of physical impairment are greater in HIV-infected women than they are in age- and sex-matched HIV-uninfected controls.

Aim 4: To identify modifiers and predictors of the association of HIV with physical impairment.

- Hypothesis 4.1: Among HIV-infected women in the WIHS cohort, HIV disease characteristics such as duration of HIV infection and severity of disease (as measured by CDC stage, CD4 cell count, and plasma RNA), correlate with physical impairment.
- Hypothesis 4.2: Among HIV-infected women, HIV-related opportunistic infections (such as bacterial, mycobacterial, fungal, malignancies, protozoal, viral, and neurological) and HIV-related conditions and complications (such as wasting, fatigue, decreased muscle mass) correlate with physical impairment.
- Hypothesis 4.3: Among HIV-infected women, treatment history (age at initiation, treatment history, present treatment) and side effects such as anthropometric abnormality (wasting), metabolic abnormality (bone mineral loss), lipodystrophy, nausea, anemia, fatigue, anxiety, depression, and pain correlate with physical impairment.

- Hypothesis 4.4: There is an association of age and age-related comorbidities (such as diabetes and hypertension) with physical impairment. The association will not vary by HIV status.
- Hypothesis 4.5: The association between neurocognitive deficits and physical impairment is greater in HIV-infected women than it is in HIV-uninfected women.

C. BACKGROUND

Since the advent of highly active anti-retroviral therapy (HAART), the number of older adults (≥ 50 years old) living with human immunodeficiency virus (HIV) has increased to more than 60,000 persons in the US, accounting for almost 15% of HIV/AIDS cases; this percentage is expected to grow (Mack). As a result of this convergence between HIV/AIDS and aging, health issues typically seen in those suffering from chronic diseases now present in HIV-infected adults. The natural history of HIV as a chronic disease, symptom manifestation, and competing risks from aging, drug toxicity, and comorbid conditions are pressing issues not yet characterized in HIV-infected older adults (Stoff). Few observational studies have adequately identified the effects of HAART treatment over extended periods of time and its likely interaction with various comorbidities. Even fewer studies have measured how these HIV- and age-related effects impact physical impairment, a known determinant for need for long-term care services among HIV-infected persons.

Resulting from “cumulative damage of multiple chronic disease processes that become more common and severe with increasing age,” physical impairment limits a person's ability to perform activities requiring stamina, physical exertion, strength, or high-level cognition without assistance (Lubeck; Cleary; Crystal; Black; Mendes de Leon). Moreover, “impairments in specific physical functions, such as muscle strength and balance, form an essential causal influence in the development of disability” (Mendes de Leon). Disability is historically defined as “age-associated physical disability within two domains, 1) basic self care activities known as activities of daily living (ADL) and 2) instrumental activities of daily living (IADL)” (Leveille). Given that impairment is a precursor to disability, it is, not unexpectedly, associated with increased risk for institutionalization and mortality.

How deficits in physical functioning play a role in health outcomes among HIV-infected persons has not been well characterized in the era of HAART. Few studies have quantified the association of HIV/AIDS and aging on functional status. One noted exception is the HIV Cost and Services Utilization Survey (HCSUS), a US representative probability sample of HIV-infected adults ≥ 18 years of age receiving care (N=2,836). Interviews were conducted between 1996 and 1997 to identify functional limitations such as climbing stairs, participating in vigorous activities, walking long distances, and “carrying out complex roles such as employment” (Crystal). Forty-three percent of the participants were unable to climb stairs; 26% were unable to walk less than one block. The inability to perform these tasks was more prevalent than the inability to perform self-care tasks such as bathing and dressing (14%) (Crystal).

A smaller cross-sectional study of HIV-infected adults (N=762), the British Columbia Persons with AIDS Study (BCPWA), echoed these findings, but with a higher prevalence of activity limitations and participation restrictions (Rusch). Limitations in at least one activity, such as the ability to walk one block, eat, shower or dress, occurred in 80.4% of participants. Participation restriction, representing quality of life and measured by a ten-item questionnaire, occurred in 93.2% of participants. Comparisons between rate of impairment, activity limitation and participation restriction across three categories of CD4 cell counts (≤ 200 CD4 cells/mm³, 201-500 cells/mm³ and >500 cells/mm³) showed that “among those with ≤ 200 CD4 cells/mm³, the odds of being at a higher restriction level were lower among those

on antiretrovirals ..., while odds of higher restriction were increased with higher limitation” (Rusch). Odds of higher restriction with higher limitation were also found among those with >200 CD4 cells/mm³. Identifying subgroups at highest risk of physical impairment, such as these found in BCPWA, helps inform physicians of effective treatment options, direct policy makers in planning for services, and identify factors that may be modifiable for the improvement of the quality of life of HIV-infected adults suffering from or at-risk for physical impairment. Despite the progress in estimating physical functioning and quality of life outcomes, however, issues regarding prognosis, predictors of impairment, underlying mechanisms of impairment, service needs, and therapeutic interventions that “may help HIV-infected women circumvent the functional limitations imposed by their illness” remain unexplored, particularly in the era of HAART (Osowiecki).

The focus of this project is to more systematically quantify levels of physical impairment among WIHS participants. To date, no study has been published in the HAART era that has characterized physical impairment within this unique population, nor evaluated the role of HIV-, age- and neurocognitive-related exposures. Unlike HCSUS and BCPWA, cohorts consisting mainly of middle-class white participants, the WIHS cohort consists largely of underprivileged women, with over one-half African-American. Moreover, because WIHS is one of the largest studies of the natural history of HIV in women, we can evaluate HIV-, age-, and neurocognitive-related exposures as predictors. We will also perform internal comparisons between HIV-infected and -uninfected persons, as well as conduct external comparisons using healthy seronegative women participating in either the Cardiovascular Health Study (CHS) or the Women's Health and Aging Study (WHAS). Since approximately two-thirds of WIHS participants are less than 50 years of age, we expect that mild forms of impairment will be more common than severe forms. To measure the spectrum of severity, our instruments will include assessments for frailty syndrome, instrumental activities of daily living (IADL), and the physical functioning component of the quality of life scale (QOL).

Frailty, defined as having at least three of the following five attributes – unintentional weight loss, muscle weakness, slow walking speed, exhaustion, and low physical activity – represents:

“a physiologic state of increased vulnerability to stressors that results from decreased physiologic reserves, and even dysregulation, of multiple physiologic systems ... There are numerous systems in which such physiologic decrements in mass or function have been demonstrated with age, including neuromuscular, such as sarcopenia and decrease in muscle fiber function; osteopenia; dysregulation of the hypothalamic axis, of inflammation and of immune function; and even heart rate variability. Frailty is an aggregate expression of risk resulting from age- or disease-associated physiologic accumulation of subthreshold decrements of multiple physiologic systems. Although the early stages of this process may be clinically silent, when the losses of reserve reach an aggregate threshold that leads to serious vulnerability, the syndrome may become detectable by looking at clinical, functional, behavioral, and biological markers” (Fried).

IADLs encompass both mobility and non-mobility related activities that target social and physical functioning. Examples of mobility-related activities include house management tasks such as cleaning, shopping, and managing money. Unlike ADLs, that include tasks such as bathing, getting in and out of bed or a chair, and using the toilet, mobility-related IADLs reflect a finer level of motor coordination. Previous studies have demonstrated that lack of motor coordination “may well play an intermediary role in the pathway from decline in physical functions to ADL disability” (Jette; Mendes de Leon). Such difficulties in motor

coordination like strength and balance, for example, are hypothesized to “lead ... to difficulties in ambulation, but may require more prolonged duration or increasing severity before they will affect self-care tasks less directly related to mobility (such as dressing and bathing)” (Mendes de Leon). While repeated measurements over time in prospective observational studies are necessary to tease out the sequence of events, the proposed cross-sectional study will help confirm findings from previous studies, as well as explore the effect of HIV/AIDS on the frequency and distribution of physical impairment. Future work using repeated measurements will be possible if these measures remain part of the WIHS core.

In evaluation of HIV treatment regimens, clinicians and researchers have typically relied on the QOL scale as an important health outcome with respect to physical functioning (Bozzette; Clingerman). QOL estimates the quantity, quality, and range of activities that people experience in their daily living. In a small cross-sectional study that examined the influence of neurocognitive and emotional distress and immune dysregulation among HIV-infected women (N=36), QOL was found to “depend on both the emotional state and the integrity of functional abilities” (Osowiecki). Associations with disease stage, CD4 cell count, and symptoms have also been identified (Osowiecki; Tozzi).

D. STUDY DESIGN

The three main outcomes of this study include mobility-related IADLs, frailty, and the physical functioning component of the QOL scale. The physical-functioning component of the QOL scale is already implemented in WIHS (F26) and is administered during all even-number core visits.

1. OUTCOME VARIABLES

a. Mobility-related IADLs

Participants will respond to questions about disabling symptoms that reflect mobility-related IADLs. Participants will rate their disability in each task according to four levels: 1) no difficulty, 2) some or a little difficulty, 3) a lot of difficulty, or 4) unable to do. Responses will be dichotomized such that women will be classified as either mobility-related IADL impaired or not impaired.

b. Frailty

A phenotypic assessment of frailty (Fried) has been implemented in many studies and consists of five components:

1. **Physical shrinking:** Defined as unintentional weight loss of ≥ 10 lbs in the prior year or, at follow-up, of $\geq 5\%$ of body weight in the prior year (by direct measurement of weight). Using core WIHS data, we will calculate $(\text{weight}_{\text{previous year}} - \text{weight}_{\text{current}}) / (\text{weight}_{\text{previous year}}) = K$. If $K \geq 0.05$ and the subject does not report that he/she was trying to lose weight (i.e., unintentional weight loss of at least 5% of previous year's body weight), then the participant will be categorized as frail by weight loss criterion.
2. **Poor endurance and energy:** This will be measured by self-report of exhaustion, identified by two questions from the CES-D scale. Self-reported exhaustion is associated with stage of exercise reached in graded exercise testing, as an indicator of VO2 max. Using the CES-D Depression Scale, the following statements are read: “I felt that everything I did was an effort.” “I could not get going.” And then, “How often in the last week did you feel this way?”, which is coded as:

- 0 = rarely or none of the time (<1 day)
- 1 = some or a little of the time (1-2 days)
- 2 = a moderate amount of the time (3-4 days)
- 3 = most of the time

Participants answering “2” or “3” to either of these questions will be categorized as frail by the exhaustion criterion.

3. **Low physical activity level:** A weighted score of kilocalories expended per week will be calculated based on each participant's response to the FRAM (Fat Redistribution and Metabolic Changes in HIV Infection Study) Physical Activity Questionnaire. Kcals per week expended will be calculated using a standardized algorithm. For women, those with Kcals per week <270 will be considered frail by the physical activity criterion.
4. **Slowness:** This will be measured by the time to walk 3 or 4 meters, adjusting for gender and standing height. We will require women to be timed to walk a 3 or 4 meter course. The preferable length for the walking course is 4 meters; however, if 4 meters are not available, a 3 meter course may be used instead. If a 3-meter course is not available, indicate in PBM question A1 that the measured walk was not attempted due to “other reason,” and specify the reason.

If possible, all women completing visits at the same subsite should complete the same length course. For example, site A may have subsites 1, 2 and 3. While women attending visits at subsite 1 need not complete the same distance course as those attending visits at subsite 2, all women attending visits at subsite 1 should complete the same length course.

5. **Weakness:** Defined as grip strength in the lowest 20% at baseline, adjusted for gender and body mass index. Handgrip strength will be measured by a hand dynamometer such as the JAMAR dynamometer (Model BK-7498, Fred Sammons Inc, Brookfield, IL). Grip strength will be measured three times for the participant’s dominant hand only. During testing, the participant is strongly encouraged to exhibit the best possible force. The best measure in the dominant hand will be used. The following table shows the cutoff for frailty categorization, defined by BMI:

BMI	Cutoff for grip strength (Kg): criterion for frailty
≤23	≤17
23.1 – 26	≤17.3
26.1 – 29	≤18
>29	≤21

Scoring Frailty:

- Positive for frailty phenotype: ≥ 3 of above criteria present
- Intermediate (pre-frail): 1 or 2 criteria present
- Robust (non-frail): 0 criteria present

c. Physical-functioning Component of Quality of Life (SF-36/MOS-HIV)

Four items of the physical-functioning component of the QOL are included on the WIHS Psychosocial Measures form (F26), question B7. Additional items will be included on the F26a form to be implemented for visit 22 only. Scores across each item will be summarized as a continuous variable.

2. EXPOSURE VARIABLES

All exposure variables are already included in the WIHS instrument. The following variables are of particular interest to the proposed study:

a. HIV-related variables

History of AIDS-defining illness, age at HAART initiation, treatment history, current treatment, history of HIV-related comorbidity, CD4 cell count including nadir, plasma HIV RNA viral load, and clinical symptoms

b. Age-related variables

Current age, cancer diagnoses, and cardiovascular disease such as stroke, hypertension, diabetes and coronary artery disease

c. Neurocognitive-related variables

Trail-making tests and symbol digit modalities, Wide Range Achievement Test-version 3 for reading English reading level, Word Accentuation Test (WAT) for Spanish reading level, and the Wechsler Test of Adult Reading (WTAR)

d. Other variables

Race/ethnicity, illicit drug use, pregnancy, history of HCV and HBV, weight, intentional weight loss

E. PARTICIPANT ELIBILITY AND ENROLLMENT

This study, characterizing physical impairment, will be nested within the WIHS. The study design is cross-sectional; all women participating in Visit 22 (beginning on 04/01/05) of WIHS will be asked to respond to questions related to physical impairment as well as to perform simple physical activities like walking and gripping an object with their hands.

F. SUPPLIES NEEDED

- Assessment of Physical Functioning (WIHS form F26a); English or Spanish version
- FRAM Physical Activity Questionnaire (WIHS form PAQ), response cards #1 – 3; English or Spanish version
- Performance-based Measures (WIHS form PBM), QxQs; English or Spanish version
- 3-meter measuring tape (to be supplied by WDMAC)
- Jamar dynamometer (to be supplied by WDMAC)
- Stop watch
- Tape, to mark measured walk course

G. PROCEDURES

1. QUESTIONNAIRE ADMINISTRATION

- a. The Assessment of Physical Functioning (F26a) consists of 20 questions that ask about disabling symptoms that reflect mobility-related instrumental activities of daily living (IADL). F26a will be administered once per participant only, during WIHS visit 22, preferably at the participant's core visit. **F26a can be administered at any point during the interview.**

If more convenient, and agreed upon by the participant, the questionnaire can be administered during a separate visit to the clinic subsequent to the core visit (e.g., during a PK or cardiovascular substudy visit); however, no extra incentive will be provided.

- b. The FRAM (Fat Redistribution and Metabolic Change in HIV Infection) Physical Activity Questionnaire (PAQ) will be administered once per participant only, also during WIHS visit 22, preferably at the core visit. **The PAQ can be administered at any point during the interview.**

If more convenient, and agreed upon by the participant, the questionnaire can be administered during a separate visit to the clinic subsequent to the core visit (e.g., during a PK or cardiovascular substudy visit); however, no extra incentive will be provided.

In **Chicago** and **San Francisco**, many women will have completed the PAQ as part of another substudy prior to visit 22. These women need not complete the PAQ a second time; sites should enter the already collected data into Apollo, indicating the date and visit number during which it was originally completed.

2. PERFORMANCE-BASED MEASUREMENTS

The assessment of physical performance incorporates aspects of strength, mobility, freedom of movement, balance and coordination. These exams have been taken from procedures used in the NHANES (National Health and Nutrition Examinations Survey) and the EPESE (Established Population for the Epidemiologic Studies of the Elderly) studies.

The performance-based measurements can be administered at any point during the interview. If more convenient, and agreed upon by the participant, the measurements can be administered during a separate visit to the clinic subsequent to the core visit (e.g., during a PK or cardiovascular substudy visit); however, no extra incentive will be provided. Interviewers and clinicians will be trained to administer the individual components of the exam in the following sequence:

1. Explain the procedure to the study participant using a standardized script.
2. Demonstrate the procedure to the study participant.
3. Ask the participant if she has any questions.
4. Briefly explain the procedure once again.
5. Ask the study participant to perform the procedure.
6. All timed procedures are begun with the words, **“Ready? Go!”**

Results from administration of the measurements will be recorded on the Performance-based Measurements form (PBM). See the QxQs for instructions regarding how to complete specific questions on the form.

- a. **Measured Walk:** A walking course of 3 or 4 meters is identified and the beginning and ending points are marked on the floor with highly visible tape. The course should be free of obstacles. The participant will be asked to perform the measured walk two times. The preferable length for the walking course is 4 meters; however, if 4 meters are not available, a 3 meter course may be used instead. If a 3-meter course is not available, indicate in PBM question A1 that the measured walk was not attempted due to “other reason,” and specify the reason.

If possible, all women completing visits at the same subsite should complete the same length course. For example, site A may have subsites 1, 2 and 3. While women attending visits at subsite 1 need not complete the same distance course as those attending visits at subsite 2, all women attending visits at subsite 1 should complete the same length course.

First, read the instructions for completion of the task to the participant; then demonstrate how to complete the task; and finally ask the participant to perform the task.

Script for first attempt: “In this test, I would like you to walk at your usual pace from this line to the line at the end of the hall. Do you think you could do that? Good. Can you see the tape? Good. Let me demonstrate what I want you to do.”
(Demonstrate for the participant.)

“To do this test, place your feet with your toes behind, but touching, the line where we start. I will time you. When I say ‘**Ready, go!**’ walk at your usual pace to the line at the end of the hall. I will walk with you.”

When the participant is properly at the line, say “**Ready, go!**” and start the stopwatch as the participant begins walking; keep the stopwatch behind the participant so she can’t see it. Your arm can provide support if the participant loses balance. Stop the stopwatch when the participant’s first foot is completely across the finish line. Be certain to count and record the individual steps that the participant takes.

The participant will then be asked to perform the measured walk a second time.

Script for second attempt: “Now, I’d like you to try this test a second time. When I say “**Ready, go!**” walk at your usual pace to the line at the end of the hall. I will walk with you.”

When the participant is properly at the line, say “**Ready, go!**” and start the stopwatch as the participant begins walking; keep the stopwatch behind the participant so she can’t see it. Your arm can provide support if the participant loses balance. Stop the stopwatch when the participant’s first foot is completely across the finish line. Be certain to count and record the individual steps that the participant takes.

The participant will be allowed only two attempts at completing the measured walk unless there is external influence that interrupted her during the walk. For example, if the participant trips on her own during the first attempt, it will be recorded as such on the PBM and she will then go on to perform her second attempt. However, if during either of her attempts, she trips due to interference from another person, she may repeat that attempt.

- b. **Grip Strength:** The dynamometer should be set at “2” strength for testing of all participants. The computer default for this item is “2.” The participant’s chair should be at the proper height so that her arm can rest comfortably on the table at a right angle. The dynamometer also should rest on the table. A towel or pad should be placed under the arm.

Script: “In this exercise, I am going to use this instrument to measure the strength in your hands.”

SPECIAL NOTE: The grip strength examination is used to test how strong the participant’s hands are. Participants with one or more of the following conditions should not be tested:

1. Acute flare-up of wrist/hand; for example, arthritis, tendonitis or carpal tunnel syndrome.
2. Less than 13 weeks after surgery for fusion, arthroplasty, tendon repair or synovectomy of the upper extremity.
3. If the technician has concerns that this test may exacerbate symptoms of heart disease (e.g., angina), the situation should be investigated. Ask the participant if she is currently having symptoms from heart problems. This does NOT exclude the participant from the grip strength test. Local procedures should be developed to assure safety for the participant in this situation.

Read the instructions for completion of the task to the participant, demonstrate, and ask the participant to perform the task.

Script: “I’d like you to take your dominant arm, place your forearm on the table, and grab the two pieces of metal together like this.” (Examiner should demonstrate at this point.) “When I say “**squeeze,**” squeeze as hard as you can. The two pieces of metal will not move but I will be able to read the force of your grip on the dial. I will ask you to do this three times. If you feel any pain or discomfort, tell me and we will stop.”

Demonstrate to the participant.

“Now you should place your arm on the table at right angles to your body. Grip the two pieces of metal with your dominant hand. Your wrist should be straight. Ready? Go!”

Be sure to coach: “**Squeeze, squeeze, squeeze!**” Also, be sure to tell the participant when to “**Stop!**”

Repeat the examination three times in the dominant hand. Record the results of each trial before the next attempt.

H. DATA TRANSMISSION TO WDMAC

Forms F26a, PAQ and PBM will be entered into the Apollo data management system. These data will be edited, cleaned and incorporated into the WIHS Database with other visit 22 data.

In **Chicago** and **San Francisco**, many women will have completed the PAQ as part of another substudy prior to visit 22. These women need not complete the PAQ a second time; sites should enter the already collected data into Apollo, indicating the date and visit number during which it was originally completed.

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