Women's Health Initiative
Clinical Trial and Observational Study

Annual Progress Report
September 1, 1996 to August 31, 1997

Official Version

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WHI Annual Progress Report

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Executive Summary

The Women's Health Initiative (WHI) Clinical Trial and Observational Study (OS) was put into the field on September 1, 1993. Vanguard Clinical Centers (VCCs) began recruitment into the Clinical Trial (CT) component at that time. The OS proceeded upon receipt of OMB approval, and was officially opened for enrollment on September 1, 1994. The 24 new Clinical Centers (NCCs) were named in September 1994. Recruitment for both the CT and OS was officially opened for NCCs on February 1, 1995.

As of August 31, 1997, 54,469 women had been randomized into the CT, representing 21,329 Hormone Replacement Therapy (HRT) randomizations (88% of cumulative goal) and 39,722 Dietary Modification (DM) randomizations (96% of cumulative goal). Randomizations into the Calcium and Vitamin D (CaD) component, designed to occur at a CT participant's first annual follow-up visit, began on June 15, 1995, in VCCs and in February 1996 for NCCs. At this time, 16,411 women have been randomized (63% of cumulative design-based goal). In addition, 67,845 women have been enrolled in the OS.

Recruitment in the last six months has been above goal for HRT and DM, putting both of these components on track to complete randomizations by July 31, 1998. OS recruitment, while a secondary priority, is proceeding at an acceptable pace and will likely increase when some of the intensive screening for CT is finished. CaD recruitment continues to lag. A recent introduction of a swallowable formulation is expected to improve these rates somewhat. This topic, in conjunction with CaD adherence is one of the primary problems under analysis and discussion by the Program.

The age distribution has seen a small shift to older age groups. Closing younger age cells to further recruitment studywide has had a small effect and will continue to improve the agreement between the design assumptions and study performance. Nevertheless some shortfall in the 70-79 year old age range is anticipated. Minority recruitment has increased and is currently at 18% for the CT and 14.5% of OS.

Adherence to the HRT study is somewhat lower than original projections. Approximately 9.6% of HRT women have discontinued study hormones after one year and 18.6 after 2 years as compared to design assumptions of 8.8% and 14.2% respectively. Early Year 3 data indicate the subsequent drop-out rates may be somewhat smaller. Power calculations indicate that the adherence pattern suggested by the current data would reduce the power by 8%-10%. Intensive efforts are underway to understand the factors related to adherence and identify cost-efficient methods to improve it.

Intervention activities in the DM study are progressing well. Process measures of attendance at group sessions, completion of self-monitoring activities and self-reported scores for nutrient intake suggest that the current implementation is generally consistent with feasibility study results. Baseline percent calories from fat averages based on food records is lower than anticipated (about 33%) and adherence in the Intervention arm is also somewhat less than expected. Accordingly, the Control minus Intervention (C-I) difference achieved at one year is smaller than anticipated (11.2%). In September 1995, the self-monitoring goals were adjusted in an attempt to help achieve the desired intervention effect. This change may increase the C-I difference by about .8 % at one year.

Multivariate analyses have identified various program factors as well as age and racial/ethnic Minorities to be predictors of poorer adherence. The program is examining potential methods for bringing additional improvement in the C-I difference at Year 1 and in strengthening the long-term adherence for all Intervention women, with additional assistance for Minority women in particular.

Adherence to CaD supplements is of great concern as it is clearly lower than expected, with a drop-out rate of 15.1% at one year of follow-up and 26% at Year 2. The new tablet formulation is expected to improve these rates somewhat. The protocol change to add a 4-week phone call is showing a modest effect on adherence. Power for the combined fractures outcome remains high even with the anticipated reductions in adherence and sample size, but improvements in current trends will be needed to preserve adequate power for the designated primary outcome, hip fractures.

OS follow-up is proceeding well with acceptable return rates to mailings. Planned clinic follow-up of non-respondents appears adequate to achieve study goals for completeness of follow-up.

The procedures for documentation and local and central adjudication of outcomes continue to be refined. Central adjudication activities are proceeding. Event rates by study component, age and ethnicity are shown in this report for self-reported events. A summary of locally and centrally adjudicated outcomes and the corresponding agreement rate are also provided.

The PMC has been pro-active in addressing program concerns regarding clinic performance, particularly with regard to adherence and outcomes during this past year. Their activities are documented in this report.

Finally, reports on program Publications and Ancillary studies are presented.

1. Preliminary Remarks

This report documents study activities of the Women's Health Initiative (WHI) Clinical Trial (CT) and Observational Study (OS) during the period September 1, 1996 to August 31, 1997 as well as the cumulative experience. Topics include recruitment, follow-up, intervention monitoring, safety, outcomes, data quality, study timeline, design related issues and related scientific efforts. Updates are provided for each study component separately.

During this period, major milestones and emphases included:

- Successful completion of recruitment in six VCCs; closing recruitment for women under 60 years of age;
- Retention and adherence to all CT components;
- Significant improvement in the timeliness, documentation and adjudication of outcomes;
- Intensive work by the Performance Monitoring Committee (PMC) to review CC performance and provide assistance particularly on adherence and outcomes procedures;
- Analyses of baseline data;
- Completion of the analyses for the descriptive paper on the "half-way" baseline data set.

All reports summarize Clinical Center (CC) data provided to the CCC by August 31, 1997. All data presented are derived from WHILMA, the study database. Data managed in WHILMA are those defined by standardized data collection procedures and instruments (see *WHI Manuals, Vol. 2 - Procedures and Vol. 3 - Forms*).

Table 1.1 - Database Abbreviations for WHI CCs displays the abbreviations used in database reports to identify CCs. Other organizations providing data to this report are:

- McKesson (formerly Ogden) BioServices, Rockville, Maryland, CCC subcontractor for specimen repository and drug distribution (Harrison Hoppes, PhD, President).
- Epicare, Bowman Gray School of Medicine, Winston-Salem, North Carolina (formerly Epicore, located at University of Alberta, Alberta, Ontario) CCC subcontractor for central reading of electrocardiograms (Pentti Rautaharju, MD, Principal Investigator).
- University of California, San Francisco, CCC subcontractor for central reading of bone densitometry (Steven Cummings, MD, Principal Investigator).

We note that during the last year, Dr. John Foreyt, Principal Investigator of the NCC at Baylor College, Dr. Cheryl Ritenbaugh, Principal Investigator of the VCC at the University of Arizona, and Dr. David Sheps, Principal Investigator of the NCC at the University of North Carolina, Chapel Hill have stepped down from their positions to pursue other activities. Drs. Jennier Cousins, Tamsen Bassford, and Barbara Hulka have assumed the leadership roles in these Clinical Centers. We thank our former colleagues for their efforts in developing their Clinical Centers and for their contributions through various committees.

Table 1.1
Database Abbreviations for WHI CCs

Abbreviation	CC Institution and Location	Principal Investigator
Vanguard Clinical Centers (VCCs):		
ATLANTA	Emory University Atlanta (Decatur), Georgia	Dallas Hall, MD
BIRMING	University of Alabama at Birmingham Birmingham, Alabama	Albert Oberman, MD MPH
BOWMAN	Bowman Gray School of Medicine Winston-Salem(Greensboro), North Carolina	Gregory Burke, MD MS
BRIGHAM	Brigham and Women's Hospital Boston (Chestnut Hill), Massachusetts	Joann Manson, MD DrPH
BUFFALO	State University of New York, Buffalo Buffalo, New York	Maurizio Trevisan, MD MS
CHICAGO	Northwestern University Chicago and Evanston, Illinois	Philip Greenland, MD
IOWACITY	University of Iowa Iowa City and Bettendorf, Iowa	Robert Wallace, MD
LAJOLLA	University of California, San Diego La Jolla and Chula Vista, California	Robert Langer, MD MPH
MEMPHIS	University of Tennessee Memphis, Tennessee	William Applegate, MD
MINNEAPO	University of Minnesota Minneapolis, Minnesota	Richard Grimm, MD
NEWARK	University of Medicine and Dentistry Newark, New Jersey	Norman Lassar, MD PhD
PAWTUCK	Memorial Hospital of Rhode Island Pawtucket, Rhode Island	Annalouise Assaf, PhD
PITTSBUR	University of Pittsburgh Pittsburgh, Pennsylvania	Lewis Kuller, MD DrPH
SEATTLE	Fred Hutchinson Cancer Research Center Seattle, Washington	Maureen Henderson, MD DrPH
TUCSON	University of Arizona Tucson and Phoenix, Arizona	Tamsen Bassford, MD
UCDAVIS	University of California, Davis Sacramento, California	John Robbins, MD

Table 1.1 (continued)
Database Abbreviations for WHI CCs

Abbreviation	CC Institution and Location	Principal Investigator
New Clinical Centers (NCCs):		
CHAPHILL	University of North Carolina at Chapel Hill Chapel Hill, North Carolina	Barbara Hulka, MD, MPH
CHI-RUSH	Rush Presbyterian- St. Luke's Medical Center Chicago, Illinois	Henry Black, MD
CINCINNA	University of Cincinnati Cincinnati, Ohio	James Liu, MD
COLUMBUS	Ohio State University Columbus, Ohio	Rebecca Jackson, MD
DETROIT	Wayne State University Detroit, Michigan	Susan Hendrix, DO
GAINESVI	University of Florida Gainesville and Jacksonville, Florida	Marian Limacher, MD
GWU-DC	George Washington University Washington, DC	Judith Hsia, MD
HONOLULU	University of Hawaii Honolulu, Hawaii	David Curb, MD
HOUSTON	Baylor College of Medicine Houston, Texas	Jennifer Cousins, PhD
IRVINE	University of California, Irvine Irvine, California	Frank Meyskens, Jr., MD
LA	University of California, Los Angeles Los Angeles, California	Howard Judd, MD
MADISON	University of Wisconsin Madison, Wisconsin	Catherine Allen, PhD
MEDLAN	Medlantic Research Institute Washington, D.C.	Barbara Howard, PhD
MIAMI	University of Miami Miami, Florida	Marianna Baum, PhD

Table 1.1 (continued)
Database Abbreviations for WHI CCs

Abbreviation	CC Institution and Location	Principal Investigator
NCCs: (cont.)		
MILWAUKE	Medical College of Wisconsin Milwaukee, Wisconsin	Jane Morley Kotchen MD MPH
NEVADA	University of Nevada Reno, Nevada	Sandra Daugherty, MD PhD
NY-CITY	Albert Einstein College of Medicine PhD Bronx, New York	Sylvia Wassertheil-Smoller,
OAKLAND	Kaiser Foundation Research Institute Oakland, California	Robert Hiatt, MD, PhD
PORTLAND	Kaiser Foundation Research Institute Portland, Oregon	Barbara Valanis, DrPH
SANANTON	University of Texas San Antonio, Texas	Robert Schenken, MD
STANFORD	Stanford University San Jose, California	Marcia Stefanick, PhD
STONYBRK	Research Foundation of SUNY, Stony Brook Stony Brook, NY	Dorothy Lane, MD
TORRANCE	University of California, Los Angeles Torrance, California	Rowan Chlebowski, MD PhD
WORCESTR	University of Massachusetts Worcester, Massachusetts	Judith Ockene, PhD

2. Enrollment

2.1 Overview

Enrollment into WHI is a multistage process consisting of recruitment, screening and randomization into the CT or registration into the OS. *WHI Manuals, Vol. 1 - Study Protocol and Policies, Protocol Section 5.2. - Enrollment* describes the model screening process. A brief description is provided here for ease of reference. Clinical Centers may tailor the process to local needs, subject to the constraints of informed consent and pre-randomization baseline data requirements.

The initial contact is designed by each CC but is often conducted through a mass mailing, media event, or local presentation. Responding women are prescreened for basic eligibility using *Form 2/3 - Eligibility Screen* (self-administered format/telephone interview). Those still eligible for the HRT or DM components are invited to Screening Visit 1 (SV-1). For efficiency, many CCs ask women to complete *Form 60 - Food Frequency Questionnaire (FFQ)* to determine dietary eligibility prior to scheduling SV-1.

Women attending SV-1 are given an Initial Screening Consent and baseline screening and data collection activities common to all study components are conducted. Women who are no longer eligible for, or interested in, CT participation are invited to participate in the OS. Consent and additional OS data collection are completed, usually at the SV-1 or through mail contact immediately thereafter. Women still eligible for and interested in HRT or DM are given component-specific informed consent documents and are scheduled for Screening Visit 2 (SV-2).

Women attending SV-2 complete the appropriate CT consent forms and undergo the clinical procedures required of all CT participants (ECG, breast exams) as well as component specific requirements appropriate to their status (gynecological exam and run-in medication dispensing for HRT, Four-Day Food Record (4DFR) teaching for DM). Screening Visit 3 (SV-3) is scheduled after an interval of at least four weeks for HRT to allow assessment of the run-in period and to allow adequate time to obtain required laboratory results.

At SV-3, a final eligibility determination is conducted to assess all available clinical data, adherence and experience with the run-in for HRT, and ability to complete the 4DFR for DM. Eligible women are randomized to HRT, DM, or both, as appropriate, at this visit.

Women who become ineligible for or disinterested in CT participation at any point in the screening process are invited to participate in the OS.

Women who are randomized to either HRT or DM and are eligible for the CaD are invited to be randomized into the CaD component, typically at the time of their first annual follow-up visit.

Limitations of this report result from the following factors: (1) CCs are free to prescreen women with locally produced instruments and methods. They are neither obligated to report on this activity nor are there mechanisms in WHILMA to do so. (2) CCs are free to tailor their screening activities to local circumstances as described above, making exclusion rates by stage of screening variable among CCs. (3) CCs are not required to enter data on known ineligible women. This causes the

recruitment yields to be overestimated and the screening activities and exclusion rates to be underestimated.

2.2 Recruitment Goals

In the initial planning, NIH anticipated that 45 CCs would be funded in two phases. Sixteen VCCs were selected for phase one. In the second phase of competition only 24 sites were finally selected resulting in a total of 40 CCs. Recruitment goals and budgets were based on 45 clinics however, so the program is addressing this shortfall by asking existing clinics, particularly VCCs, to consider recruiting beyond the original goals. Ten VCCs have offered to do enhanced recruitment over an extended period and were awarded the additional funds to support this activity. Five NCCs have also been awarded enhanced recruitment. (See *Table 2.1 - Enhanced Recruitment Sites.*) In addition, clinics having the ability to over-recruit in increments less than 25% have been encouraged to do so with assurances that budgets will be adjusted accordingly at the end of recruitment.

Three NCCs have had their recruitment goals reduced: Rush Presbyterian at Chicago (to 50%), Harbor-UCLA at Torrance (to 75%) and Baylor College at Houston (to 100% from their enhanced goal of 150%). The NIH made these changes after the assessment of the Performance Monitoring Committee that these Clinical Centers would not be able to catch up to their existing goals within the defined recruitment period.

These combined adjustments to clinic goals provide the equivalent of 43.75 clinics recruiting into DM, 44.75 for HRT, and 44.25 for OS. It is anticipated that over-recruitment in the remaining clinics can account for a significant portion of the remaining deficits, particularly for DM.

Finally, in a continuing effort to emphasize CT recruitment over the OS, the monthly goals for OS were reduced by 35%. The reduction was calculated to reflect the yield for OS recruitment expected under the most efficient CT recruitment strategies. This change was made to reinforce the message that resources and strategies should be managed to optimize CT recruitment. While this does not represent a formal change in the overall expected enrollment of 100,000 in OS, some shortfall may or may not occur. Three of the six VCCs that have completed recruitment met or exceeded their OS goals and two others reached 85%, suggesting that most of the remaining CCs will approach their OS target without specific recruitment into this component (3 of the 6 ended recruitment at ≥95% of OS goal).

Table 2.1
Enhanced Recruitment Sites

		Increase	Date Initiated	Comments
Pawtucket	VCC	75%	4/1/95	
La Jolla	VCC	50%	4/1/95	Reduced minority recruitment goal to 47% overall.
Brigham & Women's	VCC	50%	4/1/95	
Minneapolis	VCC	25%	4/1/95	
Memphis	VCC	25%	4/1/95	Offered additional minority recruitment to 26% overall.
Birmingham	VCC	25%	4/1/95	Continued minority recruitment goal of 60%. Bone Density measures not required on additional participants.
Tucson	VCC	25%	12/1/95	Reduced minority recruitment goals to 52% overall.
Atlanta	VCC	25%	5/1/96	Reduced minority recruitment goals to 52% overall.
Iowa	VCC	100% HRT 50% OS	5/1/96	
Cincinnati	NCC	25%	5/1/96	
Gainesville	NCC	25%	5/1/96	
Stanford	NCC	25%	5/1/96	
Newark	VCC	50%	5/1/96	
New York City	NCC	25%	5/1/96	

2.3 Progress

VCC recruitment into the CT officially opened September 1, 1993. OS enrollment at VCCs was delayed until September 1, 1994 at which time the study obtained clearance from the Office of Management and Budget to begin OS accrual. Recruitment into both the CT and OS components officially began in NCCs on February 1, 1995.

Table 2.2 presents the current status of recruitment by study component over the past year and cumulatively. *Figures 2.1* through *2.4* display actual and design projects for quarterly recruitment into each study component throughout the recruitment period. Changes in goals indicate the start of recruitment at NCCs or the start of enhanced recruitment at selected sites. Recruitment efforts in the last few months appear particularly strong. Some of this is attributed to continued recruitment at the 6 VCCs without enhanced recruitment goals but overall it reflects a strong focus on meeting recruitment goals on time. Recruitment into HRT and DM is on track to finish randomizations by July 31, 1998. Enrollments into OS are scheduled to be completed at the same time. Though lagging somewhat in reaching the overall goal, OS recruitment has been deliberately de-emphasized to assure timely recruitment into CT. Since screening for OS is considerably easier, we are optimistic that the OS will reach goal.

Table 2.2
Component-Specific Enrollment Status
Data as of August 31, 1997

Study Component	Enrollment in last 6 months		Cumulative Enrollment			Enrollment months remaining
	N	% of goal	N	% of cumulative goal	% of overall goal	
HRT	4973	135%	21329	88%	78%	11
without Uterus	1931	112%	8407	77%	68%	11
with Uterus	3042	154%	12922	97%	85%	11
DM	7324	116%	39722	96%	83%	11
CaD	4926	64%	16411	62%	36%	23
OS	10828	88%	66108	110%	>66%	11

Figure 2.3 - HRT and DM Randomizations per Month at VCCs (a) and NCCs (b) and *Table 2.1 - Randomization Activity by Clinic Group, Study Component and Month* display monthly HRT and DM randomization activities separately for VCCs(a) and NCCs(b). The pace of studywide recruitment has increased in the last few months, particularly for DM where both VCCs and NCCs have been able to exceed their monthly goals.

We note a slightly smaller overlap in DM and HRT participation. The design assumed that approximately 17% of CT participants would be randomized to both HRT and DM. The observed value is 12.1%. Using this value and holding fixed the sample size in each of these components, we project that the overall CT sample size will increase from 64,500 to 67,400.

Recruitment of HRT participants continues to favor those with an intact uterus, currently 61% compared to the design assumption of 55%. Because of the greater prevalence in CHD risk factors among hysterectomized women, which will likely improve the power, we have elected not to compensate for this imbalance in the recruitment process by lowering the goal for hysterectomized women. As recruitment continues to focus on the older groups, the proportion who have had a hysterectomy is likely to increase.

Recruitment into CaD requires further comment. The randomization to CaD lags the other trial components by one year, meaning any delay in the primary randomization forces a delay in CaD. The original design assumed that 70% of CT women would agree to join CaD. Our current experience suggests that this number is about 54%. The one important reason for not joining that we have identified is the current CaD formulation (chewable). A new, swallowable formulation has been obtained from the manufacturer and this is being provided to CCs to offer women as an alternative. The effects of this change on recruitment should be observable in a few months time. With the increased sample size for CT overall, the current experience would yield a sample size of over 36,000. An increase in yield to 60% would result in a CaD sample size of 40,400.

The age distribution in CT is a key component of study power because some of our primary outcomes are quite age-dependent. *Table 2.3* presents the current age distribution and corresponding goals for each component.

Table 2.3
Age - Specific Recruitment by Study Component

	Total Randomized	% of Cumulative Goal	% of Overall Goal	Age Distribution	Design Assumption
HRT (Overall)					
50-54	3349	139	122	16	10
55-59	4632	96	85	22	20
60-69	8945	82	73	42	45
70-79	4403	73	64	21	25
HRT without Uterus					
50-54	1374	127	112	16	10
55-59	1644	76	67	20	20
60-69	3513	72	63	42	45
70-79	1876	69	61	22	25
HRT with uterus					
50-54	1975	148	131	15	10
55-59	2988	112	99	23	20
60-69	5432	91	80	42	45
70-79	2527	76	67	20	25
DM					
50-54	6859	466	147	17	10
55-59	9977	120	107	25	20
60-69	16720	90	80	42	45
70-79	6166	60	53	16	25
CaD					
50-54	3414	129	78	21	10
55-59	4214	80	48	26	20
60-69	6491	55	33	40	45
70-79	2292	35	21	14	25

To promote better adherence to the design assumptions, recruitment into HRT and DM was closed to women under age 55 on March 15, 1997 and to all women under 60 on July 31, 1997. Randomizations will continue for up to six months for women already in the screening process. At this time no further cell closing is anticipated. We expect that recruitment into the age 60-69 year category will reach goal but some shortfall is expected in the 70-79 year cell.

Table 2.4 presents the current enrollment by race/ethnicity for CT and OS combined. Our current level of 9805 (18%) minorities in CT indicates that we have been able to attract a large number of minority women into the component that is driving recruitment efforts. If this level of performance continues through the remaining accrual, we project 19.2% of the CT population will be from minority populations with 17.4% minority in the CT and OS combined.

Table 2.4
Ethnic-Specific Recruitment by Study Component

Minorities	CT		OS		Overall	
	N	%	N	%	N	%
American Indian or Eskimo	239	0.4	298	0.5	537	0.4
Asian or Pacific Islander	1147	2.1	1793	2.7	2940	2.4
Black or African American	5524	10.1	4889	7.4	10413	8.6
Hispanic	2355	4.3	2205	3.3	4560	3.8
Other	540	1.0	682	1.0	1222	1.0
Total Minorities	9805	18.0	9567	14.5	19672	16.3
Whites	44551	81.8	56024	84.7	100575	83.4
Unknown	113	0.2	217	0.3	330	0.3
Total	54469	100	66108	100	120577	100

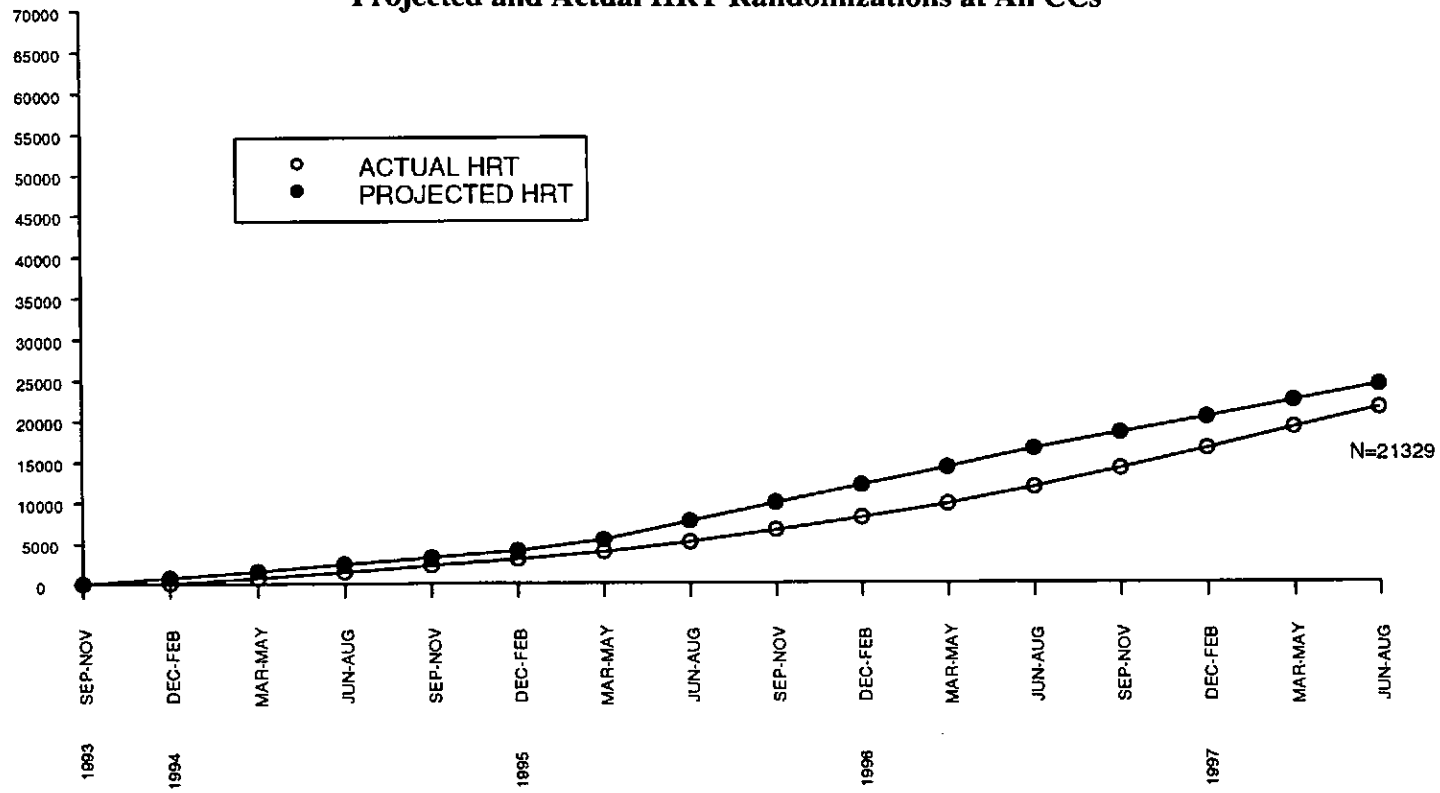
2.4 Issues

The challenges of recruiting women into WHI are large and complex. As previously reported, we face issues of identifying and attracting women into clinic, educating them in the purpose, methods, risks, and benefits of the study and the treatments involved. Clinics must conduct the recruitment effort with limited resources and sometimes with local medical community resistance to HRT, geographical constraints particularly for DM, and ambitious goals for age and ethnic minority subgroups. From the perspective of a potential study participant, WHI is complex in its multiple components and their associated entrance criteria, its many required forms and procedures, and even in its hypotheses. In particular, the objective of weighing potential benefits and risks of HRT is especially difficult to understand and possibly accept.

The differential yield and study requirements for HRT and DM have suggested that HRT recruitment could be usefully broadened to a larger catchment area. The clinics that adopted this strategy earlier showed such good results that others have been encouraged to follow suit. An informational brochure useful for HRT only recruitment was developed and provided to assist in this effort. A variety of other materials such as recruitment videos and public service announcements in both English and Spanish, and guidelines and recommendations for recruiting older women have also been developed by joint efforts of several committees, the NIH, the CCC and Porter-Novelli, a public relations firm engaged by the CCC for these activities. The PMC has also provided assistance to all sites in the form of a spreadsheet designed to help manage and project recruitment and clinic activities and a "Hot Tips" booklet which listed recommendations for recruitment and clinic operations. The PMC has also visited the clinics experiencing the most serious recruitment lags to assess the situation and provide targeted assistance.

The recruitment effort is well on track for completing HRT and DM randomizations by July 31, 1998. Though enormous energy is still required to meet the goals, the machinery is in place and we have excellent staff who are committed to the success of this program. Enrollment into OS, while a secondary priority, is expected to reach goal with no added expense for OS targeted recruitment. This is an important accomplishment of the program, assembling such a large cohort at a small marginal cost. Recruitment into CaD is our largest recruitment concern. Protocol innovations have been introduced to assist in both recruitment and adherence but it is too early yet to assess the impact of the most important change, the offering of an alternative (swallowable) CaD formulation. We will be monitoring the recruitment rate closely over the next few weeks and months to judge the impact of this option. Our success in recruiting for the other components gives us confidence that we can meet this challenge as well.

Figure 2.1
Projected and Actual HRT Randomizations at All CCs



HRT Randomizations per Quarter at All CCs

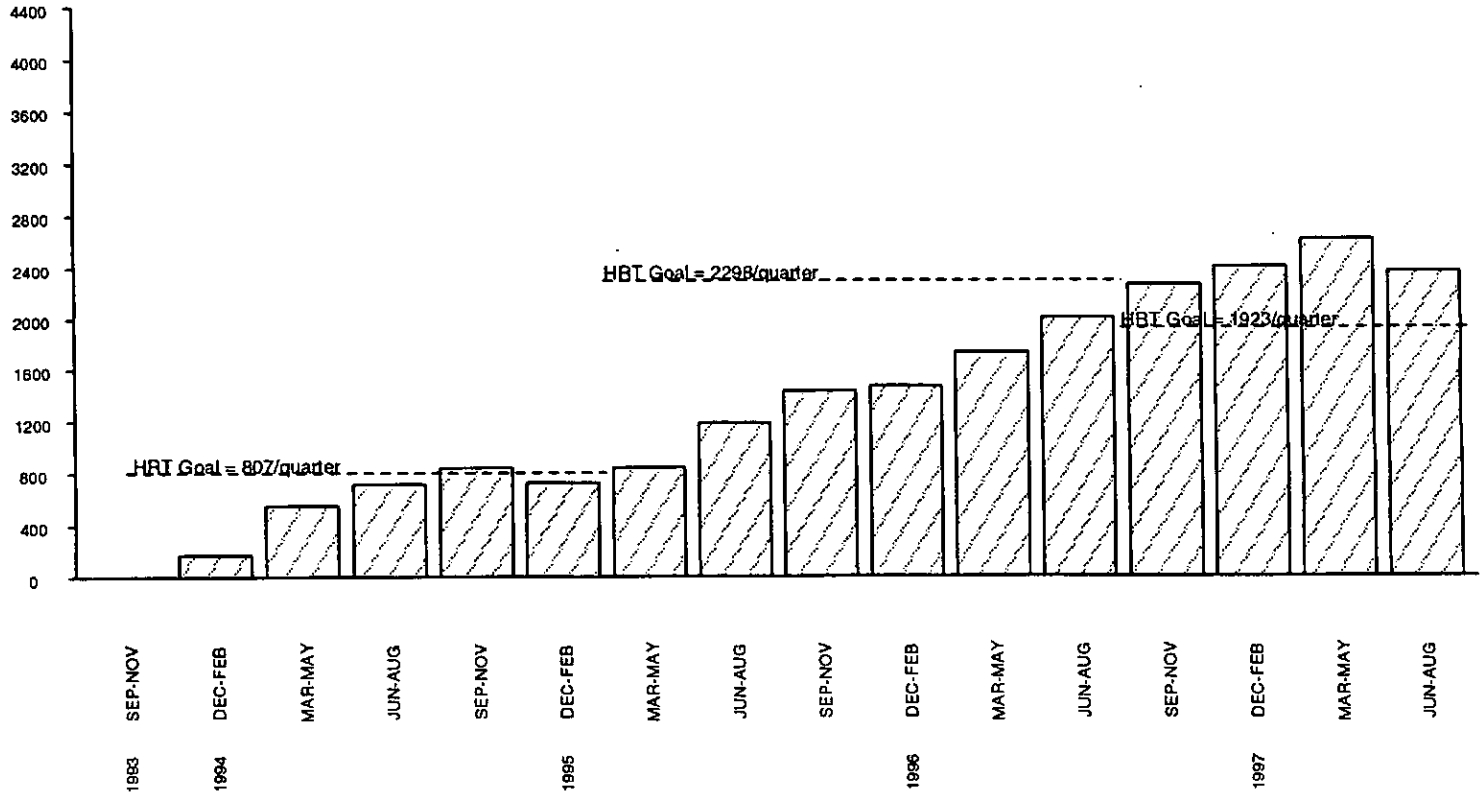
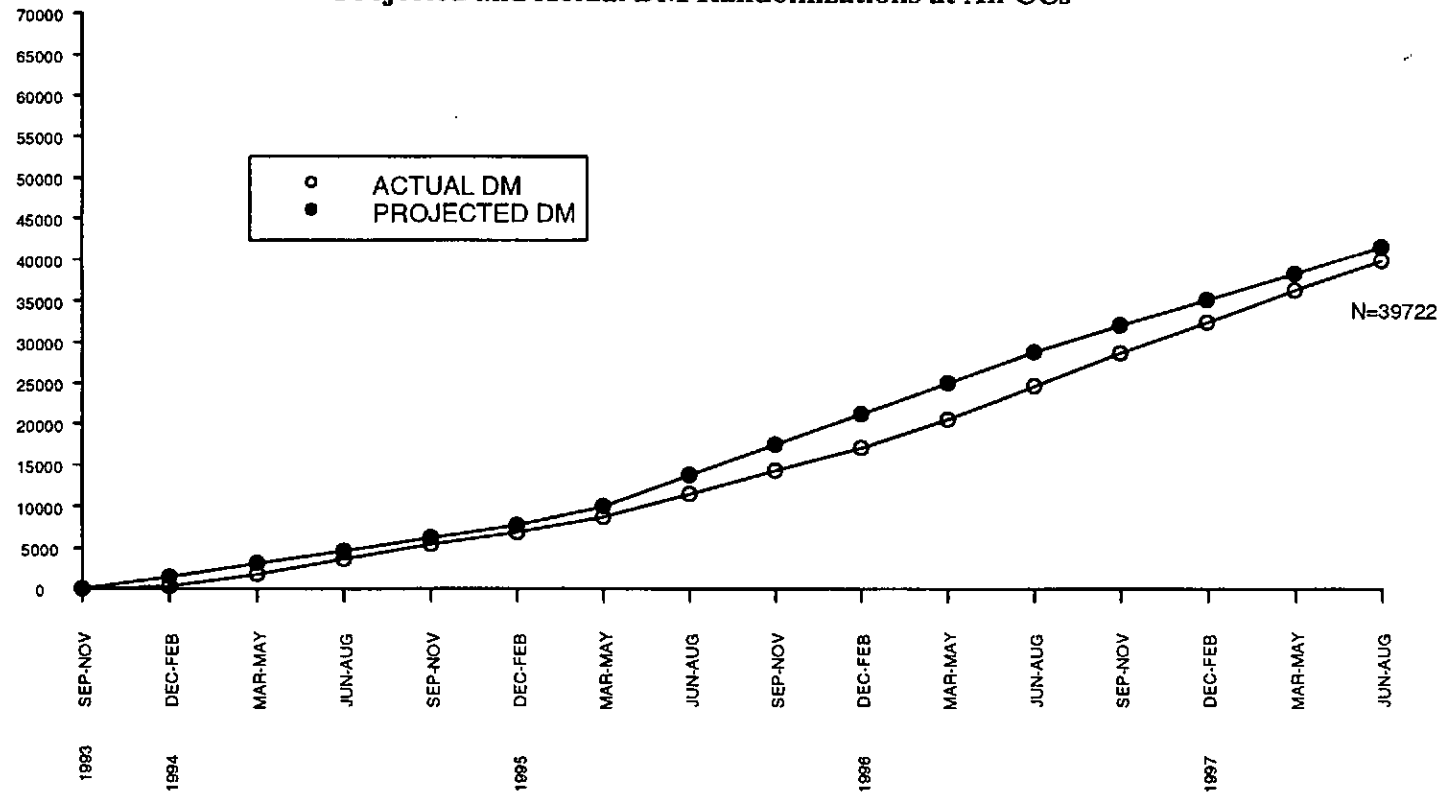


Figure 2.2
Projected and Actual DM Randomizations at All CCs



DM Randomizations per Quarter at All CCs

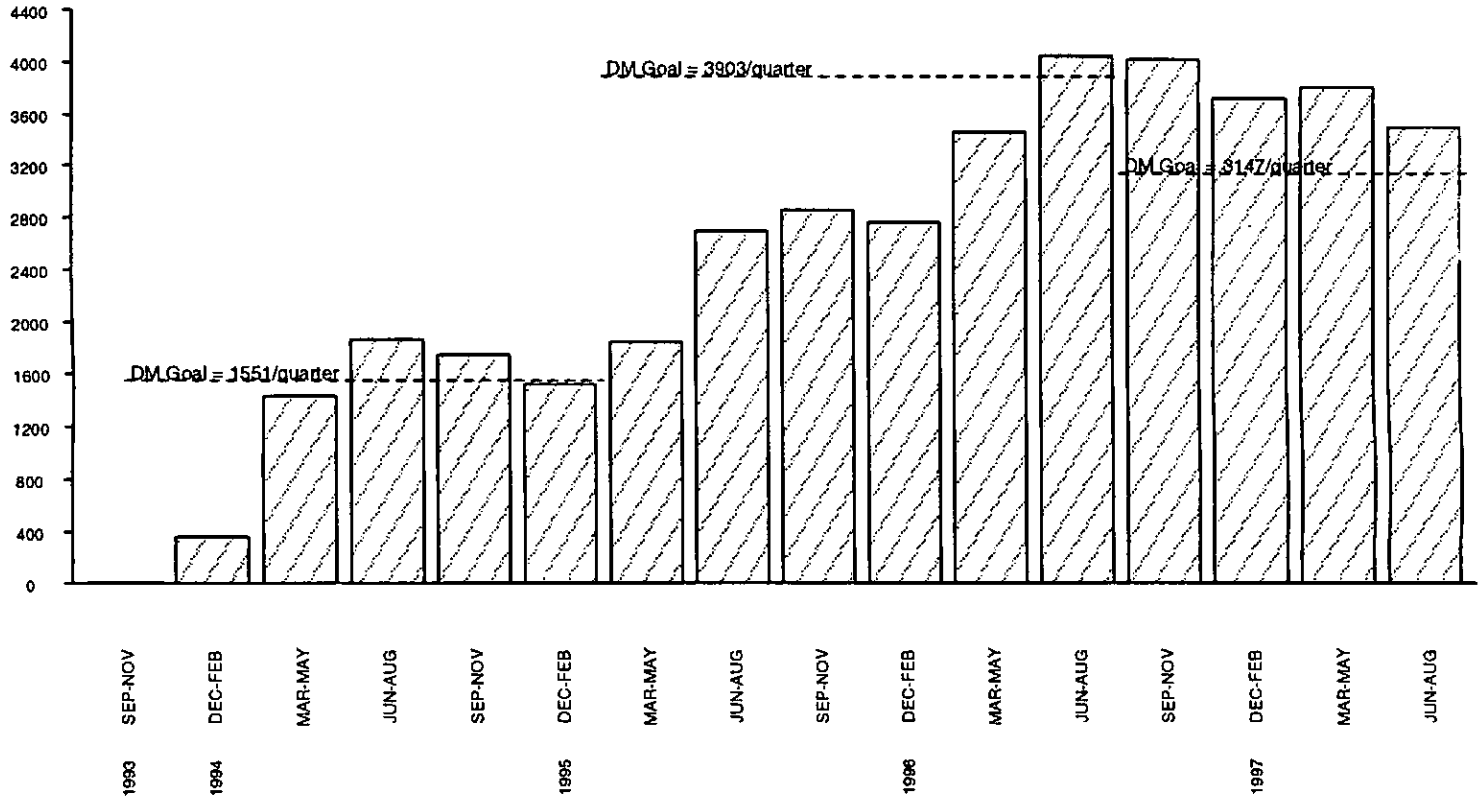
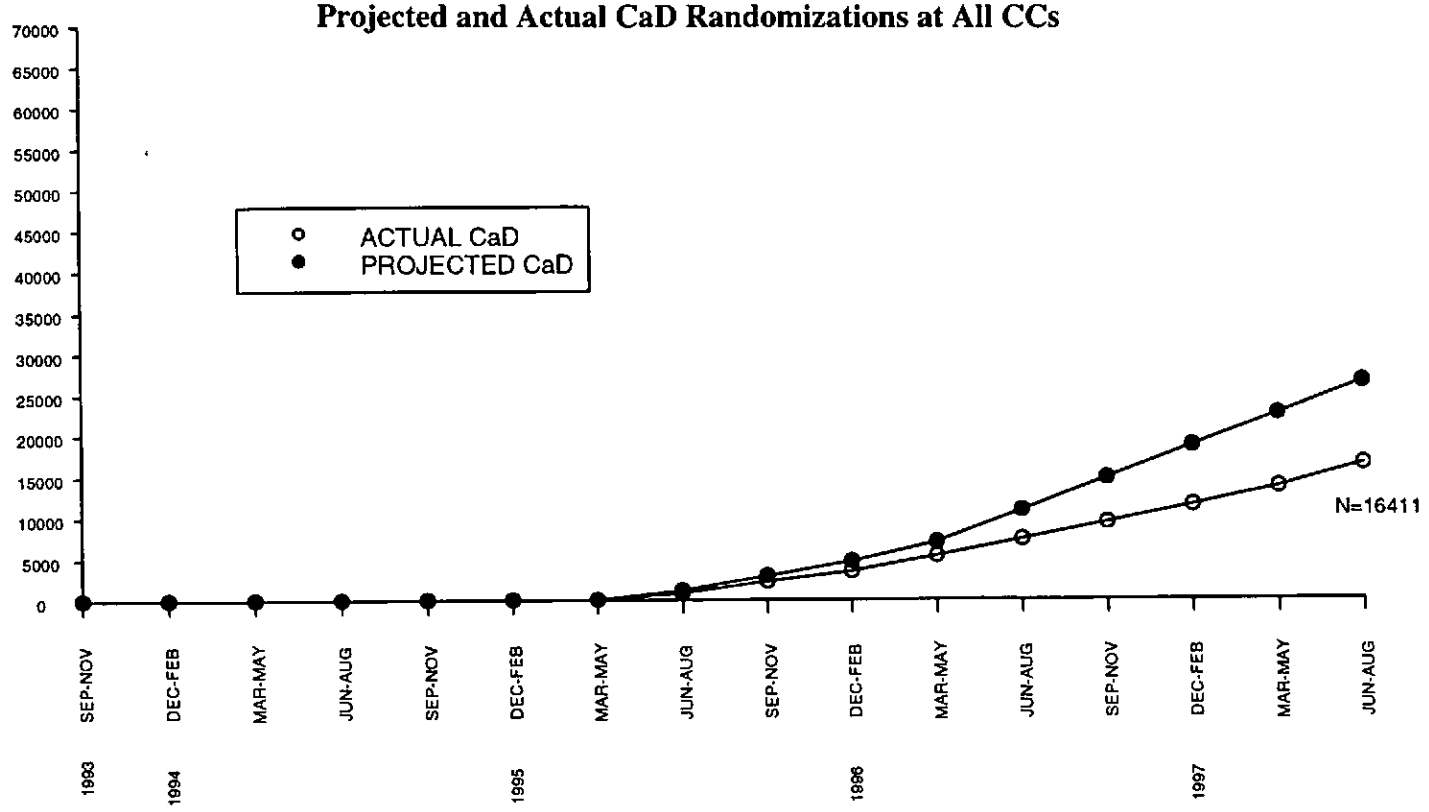


Figure 2.3
Projected and Actual CaD Randomizations at All CCs



CaD Randomizations per Quarter at All CCs

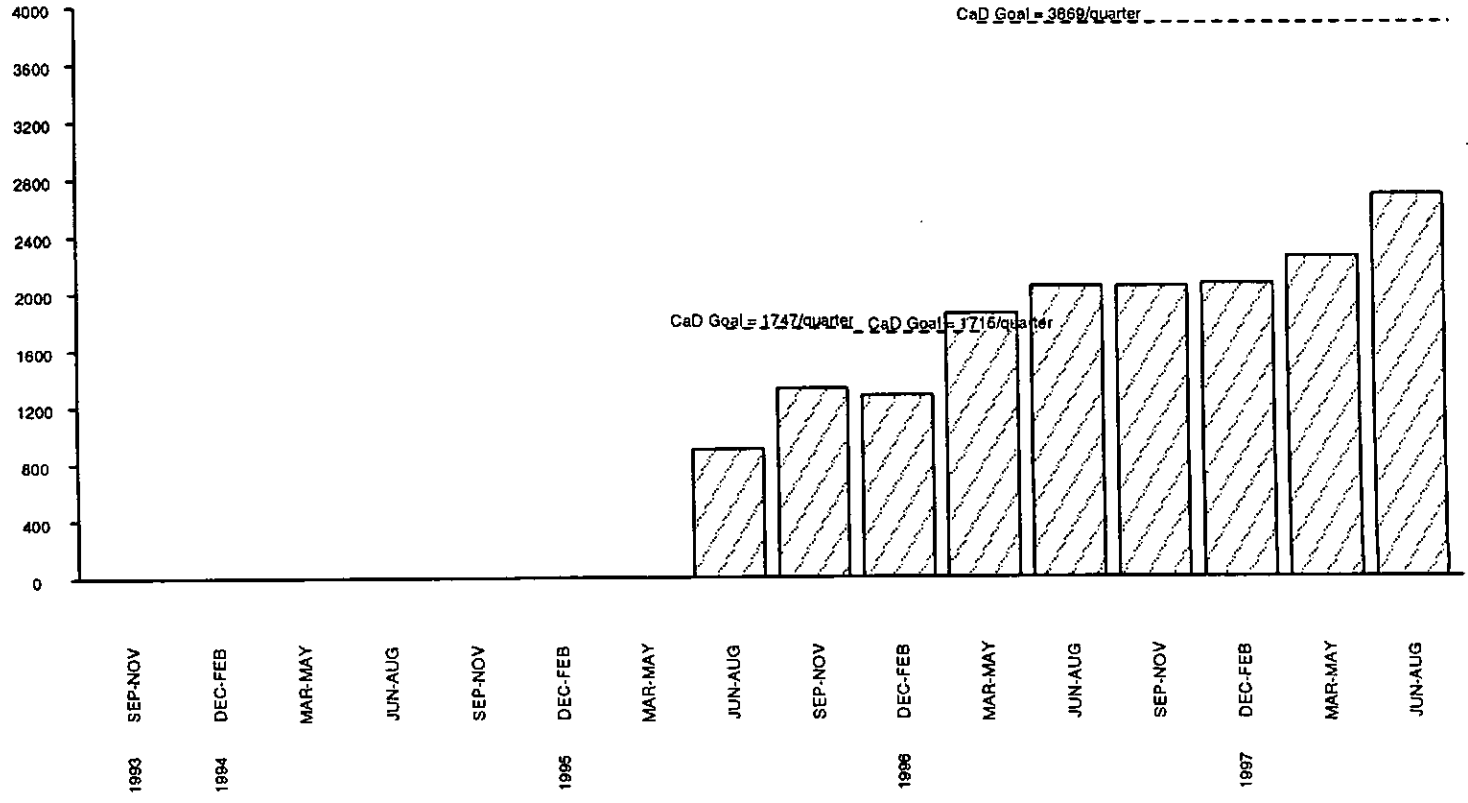
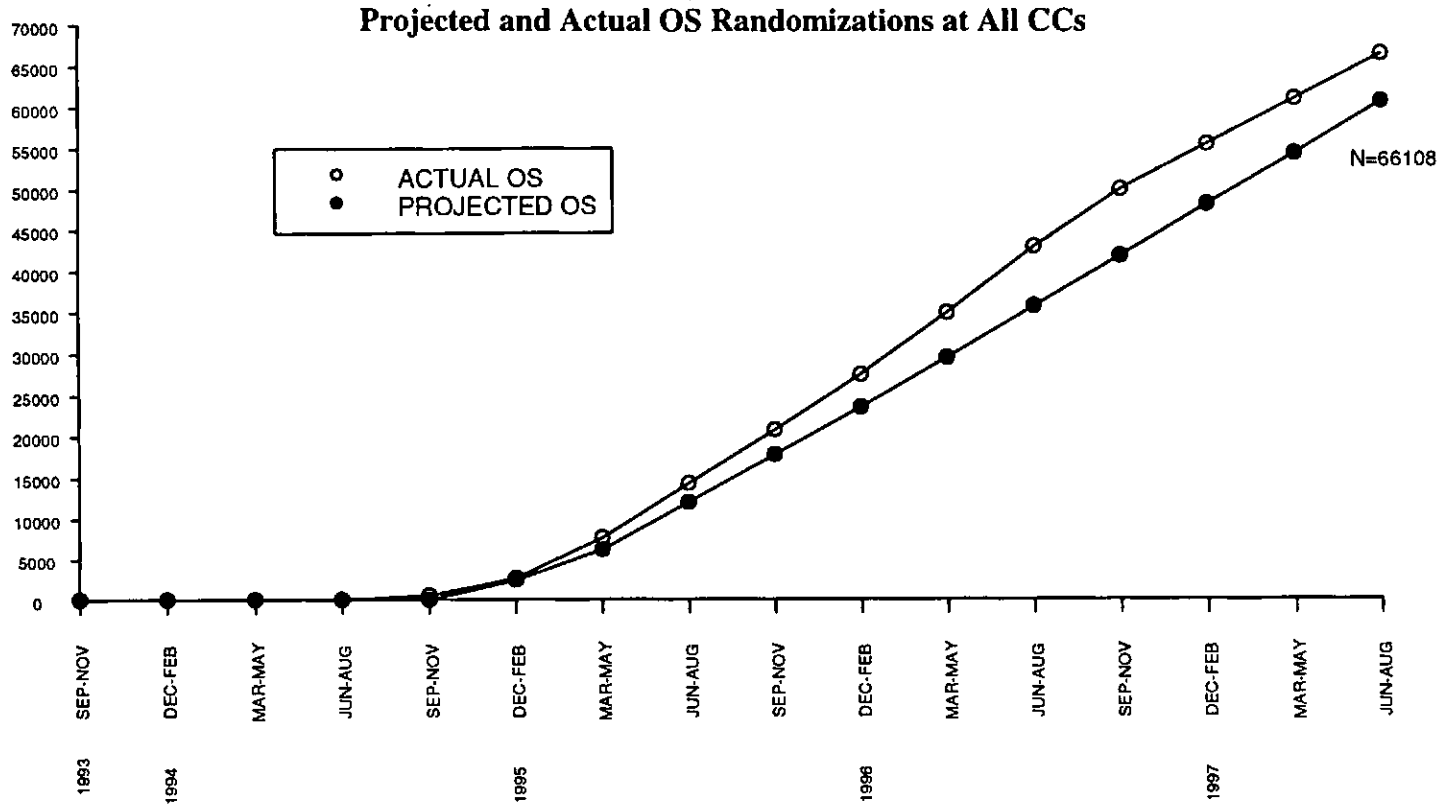
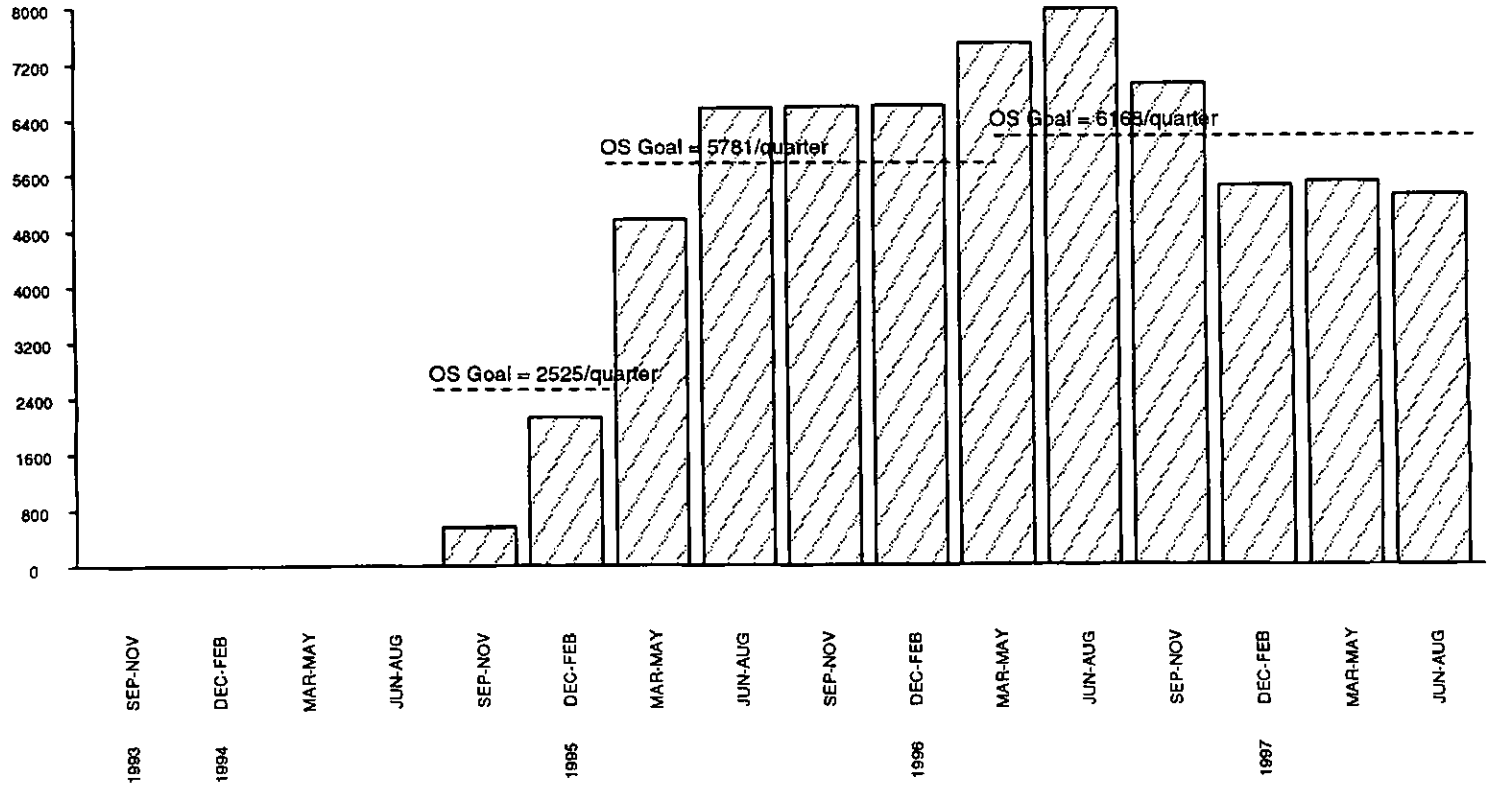


Figure 2.4
Projected and Actual OS Randomizations at All CCs



OS Enrollments per Quarter at All CCs



3. Baseline Characteristics

During the past year, the concept of a "half-way" paper was developed whereby the baseline characteristics of the first half of the CT and OS cohort would be published. A writing committee was formed (Robert Langer, Chair, Emily White, Beth Lewis, Lucille Adams-Campbell, Sandra Daugherty, Pat Elmer, Susan Hendrix, Jane Kotchen, Liza Noonan, and Maurizio Trevisan) and the CCC performed extensive descriptive analysis of the cohort accumulated through February 28, 1997. This section describes the methods used and various tables prepared for this effort.

3.1 Methods

Study participants were enrolled at 40 participating academic centers throughout the United States. All participants provided informed consent using materials approved by institutional review boards at each center. Details of the scientific rationale, eligibility requirements and other aspects of the design of the WHI have been published (Women's Health Initiative Study Group in press). General inclusion and exclusion criteria as well as specific exclusions for the DM and HRT components are outlined in *Table 3.1*.

These analyses include all women enrolled into the Clinical Trial or Observational Study between 10/1/93 and 2/28/97. There were 43,427 Clinical Trial participants and 55,278 Observational Study enrollees who entered the study between these dates.

3.1.1 Data collection and definition of variables

These data were collected as part of the WHI baseline procedures. The WHI protocol includes questionnaires and clinical measurements on all women at baseline, with some variations by the arm of the Clinical Trial (Diet Modification and Hormone Replacement Therapy) and between the Clinical Trial and Observational Study. Questionnaires include mailed self-administered questionnaires, telephone administered questionnaires and interviewer administered questionnaires in the clinics. Physical measurements, including blood pressure, height and weight, were taken during baseline clinic visits. A standardized written protocol, centralized training of clinic staff and periodic quality assurance visits by the Coordinating Center were used to assure uniform administration of instruments.

Demographic factors were based on self-report of ethnicity, education, income, marital status and living situation. The six categories for ethnicity were Native American or Alaskan Native, Asian or Pacific Islander, African American, Hispanic, White, and Other. There were relatively small numbers of women in the Native American or Alaskan Native, Asian or Pacific Islander, and Other categories. For the majority of analyses reported herein, these three groups were combined as Other. Job socioeconomic status was based on current job, or if the woman was not currently employed, the job held the longest. The managerial/professional category listed as examples jobs that generally require a Bachelor's degree, including teacher, registered nurse, and computer analyst. The other two categories were technical/sales/administrative, which primarily included office work and sales work and service/laborer, which included such work as food service and factory work.

The reproductive history included questions on number of pregnancies, livebirths, stillbirths, spontaneous miscarriages and ectopic pregnancies. Age at first birth was the woman's age at the end of her first pregnancy lasting at least 6 months. The number of induced abortions was estimated by subtracting the number of live births, stillbirths, miscarriages and ectopic pregnancies from total pregnancies.

Medical history included questions on access to medical care, use of screening procedures, health events, physician diagnoses of major diseases, and use of specified medications. History of hypertension was defined as a physician diagnosis with prescription of medication. History of diabetes was defined as a physician diagnosis that required insulin or oral medication. To be classified as hypercholesterolemic a participant had to be currently taking medication for hyperlipidemia. History of medical events was based on self report. History of cancer excluded non-melanoma skin cancer. History of a hip fracture occurring at age 55 or older excluded all women under age 55.

Smoking and alcohol intake were based on questions about past and current behavior. Former smokers were those who had ever smoked at least 100 cigarettes but did not currently smoke. Current smokers were further classified by the number of cigarettes per day currently smoked. Former drinkers were those who had ever had at least 12 alcoholic beverages in their life but did not currently drink. Current drinkers were further classified by current alcohol intake, based on the sum of beer, wine and liquor intake, adjusted for portion size, from the food frequency questionnaire (see below).

Recreational physical activity was assessed by questions on the frequency and duration of four speeds of walking and of three other types of recreational activity classified by intensity (strenuous, moderate, or light). This was summarized into episodes per week of moderate or strenuous activity of 20 minutes or more duration. This included activities with MET scores of at least 4.0 as classified by Ainsworth et al (ref), including walking "fairly fast (3.5 mph)" or "very fast (4.5 mph)", or participating in moderate or strenuous activities, such as jogging, aerobics, tennis, swimming, biking, use of an exercise machine, calisthenics, or popular or folk dancing. Those who reported no recreational physical activity were classified as no activity, those who reported some activity but none that met the criteria based on duration of at least 20 minutes, intensity at least moderate (MET score *** >=3D4.0), and frequency at least twice per week were placed in the category "limited activity", and others were classified as participating in moderate or strenuous activity 2 to <4 times per week or 4+ times per week.

Diet was assessed by a semi-quantitative food frequency questionnaire (FFQ) which was based on the questionnaire used in the Women's Health Trial: Feasibility Study in Minority Populations (Kristal), a derivative of the National Cancer Institute instrument (Block). The FFQ is divided into three sections: adjustment questions, food line items, and summary questions. The nineteen adjustment questions allow more refined analysis of fat intake (e.g., by asking about types of added fats) and fiber intake (e.g., by asking about usual types of breakfast cereals). The main section consists of questions on the frequency and portion size of 122 foods consumed over the last three months. Food items were added to incorporate regional and ethnic foods. The four summary questions ask about the usual intake of fruits, vegetables and fats added to foods and in cooking.

These questions reduce the bias toward over reporting of total food consumption when there are long lists within food groups (e.g., 25 vegetables). Nutrients are calculated based on the University of Minnesota Nutrition Coordinating Center nutrient database (Shakel). Nutrient intake excludes nutrients from supplements. The number of servings of fruits and vegetables per day was the sum of servings of fruits, fruit juices, potatoes, salads and other vegetables, based on the summary questions and individual food items. Use of supplements was ascertained by a computer-driven inventory of all nutritional supplements taken by the woman.

Depression was assessed using a self-administered eight item questionnaire for detection of depressive disorders (Burnam). Participants were asked to rate the frequency of specific depressive symptoms over the past week as well as indicate the presence of diagnostically-relevant durations of depression in the past. The weighting of the items and the cutoff for classification of depression was based on Burnam at al. Hours of sleep was the reported hours of sleep per night during the past four weeks.

Clinical measurements included blood pressure and anthropometrics. Systolic and diastolic blood pressure were each measured twice using a conventional mercury sphygmomanometer after subjects had been seated and resting for five minutes. The average of the two measurements was used for analysis. Weight was measured to the nearest 0.1 kilogram using a balance beam scale while participants were dressed in indoor clothes with shoes removed. Height was recorded to the nearest 0.1 centimeter using a wall-mounted stadiometer and a standard held-expiration technique. Body-mass index was calculated as weight in kilograms divided by the square of height in meters. The circumference of the waist at the natural waist or narrowest part of the torso and the maximal circumference of the hips were measured to the nearest 0.1 centimeter. The waist/hip ratio was computed as the ratio of these two measurements.

3.1.2 Missing data

For most variables some women had missing data. When a woman skipped a question it was generally treated as missing data, unless it was part of a list of items such as frequency of eating certain foods or performing physical activities. In these situations, the variable treated as missing only when the entire section was missing. Some variables were also treated as missing for women who completed an earlier version of a form which either did not contain this item, or did not include all of the information needed to compute the variable. Certain items that failed range or logic checks (inconsistencies between parts of questions) were also treated as missing data.

3.1.3 Statistical analyses

For categorical variables, the distribution of each variable by study arm, age, and ethnicity is given. For these variables, simple chi-square statistics were used to assess the significance of group differences. For continuous variables, means and standard deviations are given by study arm, age and ethnic group, and an analysis of variance (ANOVA) model was used to assess the significance of group differences. Interactions were tested in saturated ANOVA models that included the underlying variables and their interaction term. In these models, the response variables income and education were treated as linear.

3.2 Baseline Distributions of Key Factors

Table 3.2 presents comparisons by study component (CT and OS) as well as the combined distributions. *Table 3.3* shows comparisons among ethnic groups. *Tables 3.4* and *3.5* display ethnic comparisons within the DM and HRT components separately and *Table .6* provides the CT summary of these distributions. *Table 3.7* shows comparisons among 10 year age categories. *Tables 3.8, 3.9,* and *3.10* provide these comparisons within the DM, HRT, and CT components, respectively. *Table 3.11* shows the breaks down of Education and Income by age and ethnicity for all components combined.

3.3 References

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Table 3.1

General Inclusion/Exclusion Criteria: WHI CT and OS		
Inclusion/Exclusion Criteria	CT	OS
- Resident at least 3 years	X	X
- Willingness to provide written informed consent	X	X
- Willingness to undergo a screening procedure including measurements, blood draw, completion of forms	X	X
- No medical conditions predictive of survival time of <3 years	X	X
- Absence of conditions inconsistent with study participation and adherence (e.g., alcoholism, drug dependency, dementia)	X	X
- Participation in another randomized, controlled, clinical trial	X	X

Exclusion Criteria, CT:	DM	HRT
- Invasive cancer, anytime in past 10 years	X	X
- Breast Cancer ever or suspect breast cancer at baseline	X	X
- Acute MI, stroke or TIA in past 6 months	X	X
- Known chronic active hepatitis/sever cirrhosis	X	X
- Severe hypertension	X	X
- Use of oral corticosteroids	X	X
- Abnormal blood count (WBC, Hb, HCT)	X	X
- * Bone mineral density 3 SD below age-specific mean	X	X
- Special diet requirements incompatible with study diet	X	
- Eating 10 or more main meals per day away from home	X	
- Incapable of satisfactory completion of 4 day food record	X	
- Previous diagnosis of colon cancer	X	
- Previous diagnosis of type I diabetes	X	

Table 3.1 (continued)

Exclusion Criteria, CT:	DM	HRT
- Gastrointestinal conditions that contraindicate a high fiber diet	X	
- Previous bilateral prophylactic mastectomy	X	
- Baseline FFQ estimate of dietary percent calories from fat <32%		X
- Previous diagnosis of endometrial cancer/or endometrial hyperplasia detected at baseline		X
- Malignant melanoma		X
- Previous pulmonary embolism		X
- Non-traumatic DVT or any DVT in past 6 months		X
- Bleeding disorder		X
- Lipemic serum and/or hypertriglyceredemia		X

Exclusion Criteria, CT	DM	HRT
- Use of anticoagulant/tamoxifen		X
- Abnormal pap smear or other pelvic abnormality		X
- Severe menopausal symptoms inconsistent with assignment to placebo		X
- Known osteoporosis		X
- Unwillingness to discontinue HRT use or oral testosterone use		X
- Unwillingness to undergo baseline or follow-up endometrial aspirations		X

- In the 3 designated bone densitometry clinics only

**CaD Trial Exclusion Criteria

- Vitamin D supplementation in excess of 600 IU/day
- History of renal calculi or hypercalcemia
- Use of oral corticosteroids

** Women enrolled in either the DM or HRT are invited to participate in the CaD trial after 1 year in either the DM or HRT trial

Table 3.2

100K Paper Comparative Analysis: Clinical Trial vs. Observational Study
Data as of: 2/28/97

Variable	Clinical Trial (n=43427)		Observational Study (n=55278)		Overall (n=98705)	
	n	%	n	%	n	%
Ethnicity						
White	35608	82.0	47154	85.3	82762	83.8
Black	4487	10.3	4075	7.4	8562	8.7
Hispanic	1750	4.0	1625	2.9	3375	3.4
Other[10]	1582	3.6	2424	4.4	4006	4.1
Education						
0-8 years	704	1.6	877	1.6	1581	1.6
Some high school	1594	3.7	1813	3.3	3407	3.5
High School Diploma / GED	7669	17.8	8613	15.7	16282	16.6
School after high school	17087	39.6	19767	36.1	36854	37.6
College degree or higher	16099	37.3	23717	43.3	39816	40.7
Family Income						
< $10,000	1967	4.8	2315	4.5	4282	4.6
$10,000-$19,999	5215	12.7	6049	11.8	11264	12.2
$20,000-$34,999	10424	25.4	11874	23.1	22298	24.1
$35,000-$49,999	8651	21.1	10239	19.9	18890	20.4
$50,000-$74,999	8037	19.6	10317	20.1	18354	19.9
$75,000 +	6743	16.4	10600	20.6	17343	18.8
Job SES						
Managerial/ Professional	17042	39.9	23648	43.6	40690	42.0
Technical/Sales/Administrative	13109	30.7	15360	28.4	28469	29.4
Service/Labor	7558	17.7	9121	16.8	16679	17.2
Homemaker only	4979	11.7	6048	11.2	11027	11.4
Marital Status						
Never married	1825	4.2	2653	4.8	4478	4.6
Divorced / Separated	7135	16.5	8847	16.1	15982	16.3
Widowed	6764	15.6	9104	16.5	15868	16.1
Presently married	26780	61.9	33494	60.9	60274	61.3
Living as married	737	1.7	925	1.7	1662	1.7
Living alone	9868	22.9	14338	26.2	24206	24.7
Hysterectomy	18030	41.5	22655	41.0	40685	41.2
Age of Hysterectomy						
Never had hysterectomy	25394	58.6	32559	59.1	57953	58.9
Less than 40	6510	15.0	7118	12.9	13628	13.9
40 - 44	4214	9.7	5073	9.2	9287	9.4
45 - 49	3703	8.6	4831	8.8	8534	8.7
50 - 54	2104	4.9	3018	5.5	5122	5.2
55 or older	1390	3.2	2525	4.6	3915	4.0
Parity						
Never pregnant	3726	8.6	5773	10.5	9499	9.7
Never had term pregnancy	1145	2.7	1542	2.8	2687	2.7
1	3710	8.6	5088	9.3	8798	9.0
2	10459	24.2	14828	27.0	25287	25.8
3	10468	24.2	13242	24.1	23710	24.2
4	6859	15.9	7688	14.0	14547	14.8
5+	6847	15.8	6746	12.3	13593	13.9
HRT Ever[1]	25592	63.1	37507	69.7	63099	66.9
Health Care Provider	38709	92.0	50773	94.7	89482	93.5
Last Medical Visit within 1 Year	33094	78.7	44877	83.7	77971	81.5
High Cholesterol Requiring Pills[2]	4033	11.1	7011	13.1	11044	12.2

Table 3.2 (continued)

100K Paper Comparative Analysis: Clinical Trial vs. Observational Study
Data as of: 2/28/97

Variable	Clinical Trial (n=43427) n	%	Observational Study (n=55278) n	%	Overall (n=98705) n	%
Hypertension - Treated[2]	10621	29.0	14659	27.2	25280	28.0
MI Ever	798	1.8	1227	2.2	2025	2.1
Stroke Ever	429	1.0	753	1.4	1182	1.2
Cancer Ever[3,4]	1562	3.9	6582	12.1	8144	8.6
Breast Cancer Ever	0	0.0	2767	5.0	2767	2.8
Colon Cancer Ever[6]	49	0.1	445	0.8	494	0.5
Endometrial Cancer Ever[7]	329	0.8	989	1.8	1318	1.3
Cervical Cancer Ever[3]	474	1.2	662	1.3	1136	1.3
Ovarian Cancer Ever[3]	128	0.3	349	0.7	477	0.5
Melanoma Cancer Ever[3]	214	0.5	958	1.7	1172	1.2
Hip Fracture at Age 55+[2,9]	192	0.6	378	0.8	570	0.8
Diabetes - Treated (pills or shots)	1865	4.3	2076	3.8	3941	4.0
Smoking						
Never smoked	21793	50.7	27260	50.0	49053	50.3
Past smoker	17656	41.1	23699	43.5	41355	42.4
Smoke < 15 cigarettes / day	1790	4.2	1815	3.3	3605	3.7
Smoke 15 + cigarettes / day	1765	4.1	1719	3.2	3484	3.6
Alcohol						
Non drinker	4430	10.3	5765	10.5	10195	10.4
Past drinker	7916	18.4	10148	18.5	18064	18.4
Drink < 1 beverage / mo	5861	13.6	6361	11.6	12222	12.5
Drink < 1 beverage / wk	9118	21.2	11117	20.2	20235	20.7
Drink 1 - < 7 beverages / wk	11232	26.1	14488	26.4	25720	26.2
Drink 7+ beverages / wk	4526	10.5	7041	12.8	11567	11.8
Moderate or Strenuous Activity[8,10]						
No activity	8688	23.4	9183	16.9	17871	19.6
Some activity	14341	38.7	18466	34.0	32807	35.9
2 - 4 episodes per week	6335	17.1	10045	18.5	16380	17.9
4 + episodes per week	7699	20.8	16626	30.6	24325	26.6
Depression[5]	4616	10.9	6155	11.4	10771	11.2
Use of Supplements	26967	62.1	39128	70.8	66095	67.0

[1] Shown for Form 2 Versions 2 and 3 only (n=94586)
[2] Shown for Form 30, version 3 only (n=91294)
[3] Shown for Form 30, version 2 and 3 only (n=95669)
[4] Excluding nonmelanoma skin cancer
[5] Defined as a score of .06 or greater from the shortened CESD/DIS algorithm.
[6] CT: Applies only HRT participants who had colon cancer > 10 years ago. OS: Applies to all participants
[7] CT: Applies to only DM participants who had endometrial cancer > 10 years ago. OS: Applies to all participants
[8] Episodes defined as 20+ minutes of continuous activity. Shown for Form 34 Version 2 only (n=91562)
[9] Applies only participants 55 and older.
[10] Overall 'Other' ethnicity comprised of American Indians (n=419), Asians (n=2363), and Other / Unspecified (n=1224)
note: no statistical tests are done to determine statistical differences between OS and CT

Table 3.2 (continued)

100K Paper Comparative Analysis: Clinical Trial vs. Observational Study
Data as of: 2/28/97

	Clinical Trial (n=43427)			Observational Study (n=55278)			Overall (n=98705)		
Variable	N	Mean	SD	N	Mean	SD	N	Mean	SD
Age at Screening (yrs)	43427	61.6	7.2	55278	62.9	7.6	98705	62.3	7.4
Blood Pressure (mm Hg)									
Systolic	43424	127.3	17.5	55170	126.3	18.0	98594	126.7	17.8
Diastolic	43418	75.9	9.1	55185	74.7	9.3	98603	75.2	9.3
BMI (kg/m^2)	43264	28.8	5.8	54755	27.1	5.9	98019	27.8	5.9
Waist (cm)	43317	88.5	13.6	55037	84.4	13.6	98354	86.2	13.8
WHR	43282	0.82	0.08	54978	0.80	0.08	98260	0.81	0.08
Energy (kcal/day)	41823	1689	598.9	52656	1531	541.9	94479	1601	573.2
Calories from Fat (%)	41823	37.0	6.8	52656	30.4	8.6	94479	33.3	8.6
Dietary Calcium (mg)	41823	727.1	379.9	52656	754.1	412.6	94479	742.1	398.7
Vitamin D (mcg)	41823	4.6	2.8	52656	4.5	3.0	94479	4.5	2.9
Fruits and Vegetables (servings/day)	41658	3.7	1.9	52603	4.4	2.2	94261	4.1	2.1
Fiber (g)	41823	13.9	5.6	52656	15.2	6.2	94479	14.6	6.0
Typical Sleep (hrs/night)	43221	6.8	1.0	54922	6.9	1.0	98143	6.9	1.0

note: no statistical tests are done to determine statistical differences between OS and CT.

Table 3.3

100K Paper Comparative Analysis: Ethnicity
Data as of: 2/28/97

Variable	White (n=82762) n	%	Black (n=8562) n	%	Hispanic (n=3375) n	%	Other[10] (n=4006) n	%
Education**								
0-8 years	518	0.6	277	3.3	681	20.5	105	2.6
Some high school	2159	2.6	767	9.1	317	9.6	164	4.1
High School Diploma / GED	14016	17.1	1139	13.4	517	15.6	610	15.4
School after high school	30987	37.7	3278	38.7	1106	33.4	1483	37.4
College degree or higher	34506	42.0	3008	35.5	694	20.9	1608	40.5
Family Income**								
< $10,000	2402	3.1	1081	13.7	616	20.6	183	4.9
$10,000-$19,999	8754	11.3	1426	18.0	627	20.9	457	12.2
$20,000-$34,999	18964	24.4	1885	23.8	644	21.5	805	21.6
$35,000-$49,999	16322	21.0	1388	17.5	480	16.0	700	18.7
$50,000-$74,999	158959	20.4	1332	16.8	371	12.4	792	21.2
$75,000 +	15483	19.9	802	10.1	259	8.6	799	21.4
Job SES**								
Managerial/ Professional	34953	42.8	3362	41.3	799	25.0	1576	40.3
Technical/Sales/Administrative	24442	30.0	2030	24.9	771	24.1	1226	31.4
Service/Labor	12914	15.8	2081	25.5	888	27.7	796	20.4
Homemaker only	9297	11.4	677	8.3	744	23.2	309	7.9
Marital Status**								
Never married	3573	4.3	523	6.2	156	4.7	226	5.7
Divorced / Separated	12012	14.6	2611	30.8	761	22.9	598	15.0
Widowed	12969	15.7	1841	21.7	466	14.0	592	14.9
Presently married	52515	63.7	3381	39.9	1864	56.1	2514	63.2
Living as Married	1415	1.7	119	1.4	78	2.3	50	1.3
Living Alone**	20326	24.7	2507	29.8	583	17.7	790	19.9
Hysterectomy**	32908	39.8	4737	55.3	1494	44.3	1546	38.8
Age of Hysterectomy**								
Never had hysterectomy	49815	60.3	3824	44.8	1879	55.9	2435	61.3
Less than 40	10361	12.6	2175	25.5	591	17.6	501	12.6
40 - 44	7473	9.1	1121	13.1	349	10.4	344	8.7
45 - 49	7031	8.5	856	10.0	307	9.1	340	8.6
50 - 54	4376	5.3	364	4.3	158	4.7	224	5.6
55 or older	3515	4.3	194	2.3	77	2.3	129	3.3
Age at First Birth**								
Never been pregnant	8128	10.7	670	9.2	268	10.0	433	12.3
Never had term pregnancy	1969	2.6	511	7.0	91	3.4	116	3.3
Less than 20	9039	11.9	2237	30.8	585	21.9	399	11.3
20-24	32168	42.3	2320	31.9	1016	38.0	1242	35.3
25-29	18483	24.3	1027	14.1	479	17.9	901	25.6
30 or older	6194	8.2	510	7.0	236	8.8	427	12.1
Number of Pregnancies**								
Never pregnant	8128	9.9	670	7.9	268	8.1	433	10.9
1	5649	6.9	866	10.2	212	6.4	315	7.9
2	16723	20.3	1498	17.6	462	13.9	837	21.0
3	19085	23.1	1565	18.4	621	18.7	916	23.0
4	14200	17.2	1359	16.0	579	17.4	686	17.2
5+	18686	22.7	2532	29.8	1186	35.6	804	20.2
Number of Induced Abortions**								
Never pregnant	8128	10.4	670	8.5	268	9.2	433	11.5
Pregnant, no abortions	64529	82.6	5972	76.2	2293	79.0	2987	79.0
1	3921	5.0	700	8.9	183	6.3	239	6.3
2	1124	1.4	307	3.9	102	3.5	79	2.1
3+	434	0.6	192	2.5	55	1.9	43	1.1

Table 3.3 (continued)

100K Paper Comparative Analysis: Ethnicity
Data as of: 2/28/97

Variable	White (n=82762) n	%	Black (n=8562) n	%	Hispanic (n=3375) n	%	Other (n=4006) n	%
Parity**								
Never pregnant	8128	9.9	670	7.9	268	8.1	433	10.9
Never had term pregnancy	1969	2.4	511	6.0	91	2.7	116	2.9
1	6829	8.3	1274	15.0	296	8.9	399	10.0
2	21569	26.2	1977	23.3	652	19.6	1089	27.4
3	20600	25.0	1504	17.7	665	20.0	941	23.6
4	12440	15.1	1033	12.2	534	16.1	540	13.6
5+	10792	13.1	1520	17.9	817	24.6	464	11.7
HRT Ever[1,**]	54283	68.8	4308	51.6	1866	58.0	2642	68.1
Health Care Provider**	75923	94.3	7388	91.1	2510	79.4	3661	93.4
Last Medical Visit within 1 Year**	65882	81.9	6691	82.5	2156	68.2	3242	82.7
No Mammogram in Last 2 years**	12673	15.7	1634	20.1	916	28.9	729	18.7
No Pap Smear in Last 3 years[3,**]	4292	10.1	408	12.9	295	18.9	297	13.4
High Cholesterol Requiring Pills[2,**]	8930	11.8	1095	13.9	398	13.7	621	16.3
Hypertension - Treated[2,**]	19483	25.7	3956	50.0	682	23.1	1159	30.3
MI Ever**	1623	2.0	287	3.4	41	1.2	74	1.9
Diabetes - Treated (pills or shots)**	2494	3.0	1001	11.7	217	6.4	229	5.8
Stroke Ever**	859	1.0	200	2.3	55	1.6	68	1.7
Hip Fracture at Age 55+[2,9,**]	508	0.8	18	0.3	25	1.2	19	0.6
Smoking**								
Never smoked	40335	49.3	4165	49.6	2037	61.7	2516	63.7
Past smoker	35902	43.9	3234	38.5	1006	30.4	1213	30.7
Smoke < 15 cigarettes / day	2549	3.1	722	8.6	205	6.2	129	3.3
Smoke 15 + cigarettes / day	3052	3.7	282	3.4	56	1.7	94	2.4

Table 3.3 (continued)

100K Paper Comparative Analysis: Ethnicity
Data as of: 2/28/97

Variable	White (n = 82762) n	%	Black (n = 8562) n	%	Hispanic (n = 3375) n	%	Other[10] (n = 4006) n	%
Alcohol**								
Non drinker	6976	8.5	1484	17.6	652	19.8	1083	27.2
Past drinker	13613	16.6	2829	33.5	763	23.1	859	21.6
Drink < 1 beverage / mo	10130	12.3	1091	12.9	435	13.2	566	14.2
Drink < 1 beverage / wk	17356	21.1	1542	18.3	672	20.4	665	16.7
Drink 1 - < 7 beverages / wk	23368	28.4	1134	13.4	605	18.3	613	15.4
Drink 7+ drinks / wk	10831	13.2	370	4.4	171	5.2	195	4.9
Moderate or Strenuous Activity[8,**]**								
No activity	13698	17.9	2486	30.8	871	28.9	816	21.1
Some activity	27252	35.7	3005	37.3	1117	37.0	1433	37.1
2 - 4 episodes per week	14073	18.4	1193	14.8	422	14.0	692	17.9
4 + episodes per week	21415	28.0	1376	17.1	609	20.2	925	23.9
Use of Supplements**	57315	69.3	4215	49.2	1831	54.3	2734	68.2
Depression[5,**]**	8547	10.5	1186	14.6	622	20.6	416	10.7

OS women only

Variable	White (n = 46526) n	%	Black (n = 4025) n	%	Hispanic (n = 1586) n	%	Other[10] (n = 2388) n	%
Cancer Ever[3,4,11,**]**	5803	12.5	442	11.0	135	8.5	202	8.5
Breast Cancer Ever[11,**]**	2401	5.1	222	5.5	60	3.7	84	3.5
Colon Cancer Ever[6,11]**	375	0.8	45	1.1	13	0.8	12	0.5
Endometrial Cancer Ever[7,11,**]**	871	1.9	59	1.5	31	1.9	28	1.2
Cervical Cancer Ever[3,11]**	565	1.3	60	1.6	16	1.1	20	0.9
Ovarian Cancer Ever[3,11]**	298	0.7	26	0.7	12	0.8	13	0.6
Melanoma Cancer Ever[3,11,**]**	927	2.0	7	0.2	7	0.4	17	0.7

[1] Shown for Form 2 Versions 2 and 3 only (n=94586)

[2] Shown for Form 30, version 3 only (n=91294)

[3] Shown for Form 30, version 2 and 3 only (n=95669)

[4] Excluding nonmelanoma skin cancer

[5] Defined as a score of .06 or greater from the shortened CESD/DIS algorithm.

[6] CT: Applies only HRT participants who had colon cancer > 10 years ago. OS: Applies to all participants

[7] CT: Applies to only DM participants who had endometrial cancer > 10 years ago. OS: Applies to all participants

[8] Episodes defined as 20+ minutes of continuous activity. Shown for Form 34 Version 2 only (n=91562)

[9] Applies only participants 55 and older.

[10] 'Other' ethnicity comprised of American Indians (n=419), Asians (n=2363), and Other / Unspecified (n=1224)

[11] Applies to OS participants only.

** Indicates significant association with ethnicity at the .01 level from Chi-squared test.

Table 3.3 (continued)

100K Paper Comparative Analysis: Ethnicity
Data as of: 2/28/97

Variable	White (n=82762) N	White Mean	White SD	Black (n=8562) N	Black Mean	Black SD	Hispanic (n=3375) N	Hispanic Mean	Hispanic SD	Other[1] (n=4006) N	Other Mean	Other SD
Age at Screening (yrs)**	82762	62.6	7.4	8562	60.8	7.2	3375	59.6	6.7	4006	62.2	7.7
Blood Pressure (mm Hg)												
Systolic**	82672	126.1	17.7	8546	132.1	17.9	3374	125.8	17.0	4002	128.7	18.4
Diastolic**	82669	74.8	9.1	8555	78.1	9.5	3374	75.7	9.2	4005	77.4	9.7
BMI (kg/m^2)**	82224	27.5	5.7	8480	31.2	6.6	3342	29.0	5.8	3973	26.2	5.5
Waist (cm)**	82458	85.8	13.7	8536	91.9	13.8	3365	87.1	12.8	3995	82.2	13.1
WHR**	82377	0.81	0.08	8529	0.82	0.08	3363	0.82	0.08	3991	0.82	0.08
Energy (kcal/day)**	79998	1613	562.6	7694	1529	632.0	3012	1576	635.4	3775	1520	600.2
Calories from Fat (%)**	79998	33.1	8.5	7694	35.5	8.4	3012	34.3	8.5	3775	32.8	8.4
Polyunsaturated Fat (%)**	79998	6.7	2.4	7694	7.5	2.4	3012	6.8	2.4	3775	7.0	2.4
Monosaturated Fat (%)**	79998	12.2	3.4	7694	13.6	3.6	3012	13.1	3.8	3775	12.4	3.5
Saturated Fat (%)**	79998	11.6	3.5	7694	11.7	3.3	3012	11.6	3.3	3775	10.6	3.3
Cholesterol (mg)**	79998	213.6	118.4	7694	226.3	139.6	3012	224.5	132.9	3775	207.1	128.5
Dietary Calcium (mg)**	79998	768.3	397.9	7694	546.2	341.7	3012	716.1	412.1	3775	608.3	373.0
Vitamin D (mcg)**	79998	4.7	2.9	7694	3.8	2.7	3012	3.7	2.7	3775	3.7	2.7
Vitamin E (mg)**	79998	7.6	3.8	7694	7.3	3.7	3012	7.0	3.6	3775	7.2	3.5
Fruits and Vegetables (servings/day)**	79803	4.1	2.1	7683	3.5	2.2	3006	3.3	2.1	3769	3.9	2.1
Fiber (g)**	79998	14.9	5.9	7694	12.4	5.9	3012	13.7	6.3	3775	14.0	5.9
Typical Sleep (hrs/night)**	82412	6.9	1.0	8475	6.5	1.1	3272	6.8	1.1	3984	6.6	1.0

[1] 'Other' ethnicity comprised of American Indians (n=419), Asians (n=2363), and Other / Unspecified (n=1224)

** indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.4

100K Paper Comparative Analysis: Ethnicity for DM Randomized Participants
Data as of: 2/28/97

Variable	White (n = 26627) N	White Mean	White SD	Black (n = 3454) N	Black Mean	Black SD	Hispanic (n = 1133) N	Hispanic Mean	Hispanic SD	Other[1] (n = 1183) N	Other Mean	Other SD
Age at Screening (yrs)**	26627	61.6	7.0	3454	59.9	6.8	1133	58.7	6.1	1183	60.2	7.1
Blood Pressure (mm Hg)												
Systolic**	26624	126.5	17.2	3454	131.9	17.2	1133	125.5	16.6	1183	128.1	17.5
Diastolic**	26618	75.5	9.0	3454	78.4	9.3	1133	75.9	9.1	1183	78.4	9.5
BMI (kg/m^2)**	26545	28.6	5.5	3436	32.0	6.4	1125	29.8	5.4	1179	27.4	5.4
Waist (cm)**	26568	88.2	13.6	3445	93.5	13.3	1128	88.5	12.5	1179	84.6	13.8
WHR**	26554	0.8	0.1	3440	0.8	0.1	1127	0.8	0.1	1179	0.8	0.1
Energy (kcal/day)**	25965	1751	590.5	3303	1614	642.6	1062	1733	654.0	1158	1679	645.9
Calories from Fat (%)**	25965	38.7	4.9	3303	39.7	5.2	1062	39.1	5.1	1158	38.5	4.9
Polyunsaturated Fat (%)**	25965	7.8	2.2	3303	8.4	2.2	1062	7.7	2.2	1158	8.2	2.2
Monosaturated Fat (%)**	25965	14.3	2.1	3303	15.3	2.4	1062	15.1	2.6	1158	14.7	2.2
Saturated Fat (%)**	25965	13.7	2.6	3303	13.1	2.4	1062	13.3	2.4	1158	12.6	2.6
Cholesterol (mg)*	25965	253.0	119.8	3303	254.6	139.7	1062	263.0	125.9	1158	248.2	130.8
Dietary Calcium (mg)**	25965	752.5	369.1	3303	540.3	312.5	1062	731.3	396.0	1158	600.9	354.8
Vitamin D (mcg)**	25965	4.8	2.8	3303	3.9	2.6	1062	4.0	2.5	1158	3.9	2.7
Vitamin E (mg)**	25965	8.5	3.8	3303	8.0	3.8	1062	8.0	3.5	1158	8.2	3.8
Fruits and Vegetables (servings/day)**	25841	3.6	1.7	3299	3.1	1.8	1059	2.9	1.8	1156	3.4	1.8
Fiber (g)**	25965	14.0	5.3	3303	11.8	5.3	1062	13.6	6.1	1158	13.3	5.4

[1] 'Other' ethnicity comprised of American Indians (n=137), Asians (n=1688), and Other / Unspecified (n=853)

** Indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.5

100K Paper Comparative Analysis: Ethnicity for HRT Randomized Participants
Data as of: 2/28/97

Variable	White (n = 13175) N	White Mean	White SD	Black (n = 1690) N	Black Mean	Black SD	Hispanic (n = 932) N	Hispanic Mean	Hispanic SD	Other[1] (n = 559) N	Other Mean	Other SD
Age at Screening (yrs)**	13175	62.8	7.3	1690	60.2	7.0	932	58.7	6.2	559	62	7.4
Blood Pressure (mm Hg)												
Systolic**	13175	127.5	17.5	1690	132.4	17.6	932	126.6	16.8	559	129.8	19.3
Diastolic**	13174	75.6	9.0	1690	78.7	9.3	932	76.0	9.1	559	77.5	10.0
BMI (kg/m^2)**	13128	28.7	5.8	1679	31.6	6.5	922	29.8	5.6	557	27.6	5.6
Waist (cm)**	13139	88.9	13.9	1682	93.2	13.1	931	89.3	12.5	556	85.8	14.2
WHR**	13122	0.8	0.08	1680	0.83	0.1	930	0.83	0.1	556	0.83	0.1
Energy (kcal./day)**	12646	1627	578.5	1489	1539	638.1	802	1602	634.9	514	1533	643.1
Calories from Fat (%)**	12646	34.1	8.6	1489	35.3	8.3	802	35.4	8.1	514	33.7	8.7
Polyunsaturated Fat (%)**	12646	6.7	2.4	1489	7.4	2.3	802	7.0	2.5	514	7.1	2.5
Monosaturated Fat (%)**	12646	12.6	3.5	1489	13.6	3.6	802	13.6	3.6	514	12.8	3.6
Saturated Fat (%)**	12646	12.0	3.5	1489	11.6	3.1	802	12.0	3.1	514	11.1	3.3
Cholesterol (mg)**	12646	223.4	122.5	1489	231.3	144.1	802	236.5	140.0	514	221.8	145.4
Dietary Calcium (mg)**	12646	757.8	399.0	1489	545.7	333.5	802	702.1	394.6	514	594.4	341.3
Vitamin D (mcg)**	12646	4.7	2.9	1489	3.7	2.5	802	3.7	2.7	514	3.8	2.5
Vitamin E (mg)**	12646	7.5	3.8	1489	7.3	3.7	802	7.0	3.7	514	7.0	3.4
Fruits and Vegetables (servings/day)**	12590	3.9	2.1	1487	3.5	2.2	800	3.0	2.0	511	3.5	2.0
Fiber (g)**	12646	14.5	5.9	1489	12.3	3.0	802	13.2	6.1	514	13.2	5.7

[1] 'Other' ethnicity comprised of American Indians (n=77), Asians (n=286), and Other / Unspecified (n=196)

** Indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.6

100K Paper Comparative Analysis: Ethnicity for Clinical Trial Randomized Participants
Data as of: 2/28/97

Variable	White (n = 35608) N	Mean	SD	Black (n = 4487) N	Mean	SD	Hispanic (n = 1750) N	Mean	SD	Other[1] (n = 1582) N	Mean	SD
Age at Screening (yrs)**	35608	62.0	7.2	4487	60.0	6.9	1750	58.8	6.2	1582	60.8	7.3
Blood Pressure (mm Hg)												
Systolic**	35605	126.7	17.4	4487	132.0	17.5	1750	125.9	16.7	1582	128.7	18.1
Diastolic**	35599	75.4	9.0	4487	78.4	9.4	1750	75.9	9.1	1582	78.1	9.6
BMI (kg/m^2)**	35491	28.4	5.6	4461	31.8	6.4	1736	29.6	5.5	1576	27.3	5.5
Waist (cm)**	35523	88.1	13.6	4473	93.2	13.2	1744	88.4	12.3	1577	84.6	13.8
WHR**	35495	0.8	0.1	4467	0.8	0.1	1743	0.82	0.07	1577	0.82	0.08
Energy (kcal./day)**	34544	1705.2	587.5	4181	1590.5	645.2	1580	1665	646.9	1518	1625	640.0
Calories from Fat (%)**	34544	36.9	6.8	4181	38.1	6.8	1580	37.2	7.0	1518	36.7	6.7
Polyunsaturated Fat (%)**	34544	7.4	2.3	4181	8.0	2.3	1580	7.3	2.3	1518	7.8	2.3
Monosaturated Fat (%)**	34544	13.7	2.8	4181	14.7	3.0	1580	14.3	3.3	1518	14.0	2.9
Saturated Fat (%)**	34544	13.0	3.1	4181	12.6	2.8	1580	12.6	2.8	1518	12.0	2.9
Cholesterol (mg)**	34544	241.2	120.8	4181	245.5	140.6	1580	248.2	134.3	1518	236.6	132.7
Dietary Calcium (mg)**	34544	755.4	379.3	4181	542.9	321.9	1580	719.6	398.6	1518	598.5	352.9
Vitamin D (mcg)**	34544	4.8	2.8	4181	3.8	2.6	1580	3.8	2.6	1518	3.9	2.6
Vitamin E (mg)**	34544	8.2	3.8	4181	7.7	3.8	1580	7.5	3.6	1518	7.8	3.7
Fruits and Vegetables (servings/day)**	34392	3.7	1.9	4175	3.3	2.0	1577	2.9	1.9	1514	3.4	1.9
Fiber (g)**	34544	14.2	5.5	4181	12.0	5.6	1580	13.4	6.1	1518	13.4	5.5

[1] 'Other' ethnicity comprised of American Indians (n=184), Asians (n=897), and Other / Unspecified (n=501)

** Indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.7

100K Paper Comparative Analysis: Age at Screening
Data as of: 2/28/97

Variable	50 - 59 (n=39366) n	%	60 - 69 (n=39814) n	%	70 - 79 (n=19525) n	%
Ethnicity**						
White	31742	80.6	33849	85.0	17171	87.9
Black	4090	10.4	3256	8.2	1216	6.2
Hispanic	1876	4.8	1182	3.0	317	1.6
Other[11]	1658	4.2	1527	3.8	821	4.2
Family Income**						
< $10,000	1359	3.6	1753	4.7	1170	6.5
$10,000-$19,999	2513	6.7	4955	13.4	3796	21.1
$20,000-$34,999	6335	17.0	10207	27.5	5756	31.9
$35,000-$49,999	7181	19.3	8240	22.2	3469	19.3
$50,000-$74,999	9237	24.8	6733	18.1	2384	13.2
$75,000 +	10667	28.6	5232	14.1	1444	8.0
Job SES**						
Managerial/ Professional	18148	46.7	15622	40.0	6920	36.5
Technical/Sales/Administrative	11415	29.4	11655	29.8	5399	28.5
Service/Labor	6269	16.1	6786	17.4	3624	19.1
Homemaker only	3000	7.7	5007	12.8	3020	15.9
Marital Status**						
Never married	2009	5.1	1608	4.1	861	4.4
Divorced / Separated	7985	20.4	5972	15.1	2025	10.4
Widowed	2239	5.7	6774	17.1	6855	35.3
Presently married	25926	66.2	24806	62.6	9542	49.1
Living as Married	1031	2.6	488	1.2	143	0.7
Living Alone**	6873	17.6	9807	24.8	7526	38.9
Current Residence**						
West	11292	28.7	11633	29.2	7393	37.9
Midwest	7954	20.2	8464	21.3	3743	19.2
South	11109	28.2	9594	24.1	4125	21.1
Northeast	9011	22.9	10123	25.4	4264	21.8
Hysterectomy**	15460	39.3	16620	41.8	8605	44.1
Age of Hysterectomy						
Never had hysterectomy	23879	60.8	23169	58.4	10905	56.0
Less than 40	6780	17.3	5025	12.7	1823	9.4
40 - 44	3506	8.9	4103	10.3	1678	8.6
45 - 49	3259	8.3	3461	8.7	1814	9.3
50 - 54	1562	4.0	2120	5.3	1440	7.4
55 or older	282	0.7	1828	4.6	1805	9.3
Age at First Birth**						
Never been pregnant	4056	11.1	3362	9.4	2081	12.2
Never had term pregnancy	1429	3.9	813	2.3	445	2.6
Less than 20	6255	17.1	4727	13.2	1278	7.5
20-24	14892	40.8	15886	44.3	5968	35.0
25-29	7312	20.0	8415	23.5	5163	30.2
30 or older	2572	7.0	2659	7.4	2136	12.5
Number of Pregnancies**						
Never pregnant	4056	10.3	3362	8.5	2081	10.7
1	3309	8.4	2303	5.8	1430	7.4
2	9225	23.5	6588	16.6	3707	19.1
3	9291	23.7	8730	22.0	4166	21.5
4	6300	16.1	7295	18.4	3229	16.6
5+	7046	18.0	11368	28.7	4794	24.7

Table 3.7 (continued)

100K Paper Comparative Analysis: Age at Screening
Data as of: 2/28/97

Variable	50 - 59 (n=39366) n	%	60 - 69 (n=39814) n	%	70 - 79 (n=19525) n	%
Number of Induced Abortions**						
Never pregnant	4056	10.8	3362	9.1	2081	11.5
Pregnant, no abortions	29197	77.8	31465	85.0	15119	83.6
1	2960	7.9	1486	4.0	597	3.3
2	938	2.5	480	1.3	194	1.1
3+	391	1.0	240	0.7	93	0.5
Parity**						
Never pregnant	4056	10.4	3362	8.5	2081	10.7
Never had term pregnancy	1429	3.7	813	2.1	445	2.3
1	4170	10.7	2876	7.3	1752	9.0
2	12161	31.1	8470	21.4	4656	24.0
3	9167	23.4	10018	25.3	4525	23.4
4	4688	12.0	6886	17.4	2973	15.3
5+	3481	8.9	7165	18.1	2947	15.2
HRT Ever[1,**]	27103	72.4	24349	64.1	11647	61.7
Health Care Provider**	34982	91.7	36333	94.1	18167	96.1
Last Medical Visit within 1 Year**	29799	78.1	31771	82.3	16401	86.7
No Mammogram in Last 2 Years**	6458	16.8	6165	15.9	3329	17.7
No Clinical Breast Exam in Last 2 Yrs.[9,**]	980	4.8	1465	6.8	1134	9.4
No Pap Smear in Last 3 Years[3,**]	1773	8.6	2139	10.8	1380	14.9
High Cholesterol Requiring Pills[2,**]	2807	7.9	5172	14.2	3065	16.8
Hypertension - Treated[8,**]	7278	20.3	11162	30.6	6840	37.8
MI Ever**	355	0.9	890	2.2	780	4.0
Diabetes - Treated (pills or shots)**	1205	3.1	1809	4.5	927	4.8
Stroke Ever**	244	0.6	498	1.3	440	2.3
Hip Fracture at Age 55+[2,10,**]	23	0.1	210	0.6	337	1.9
Smoking**						
Never smoked	18785	48.2	19604	49.8	10664	55.7
Past smoker	16588	42.5	17114	43.5	7653	40.0
Smoke < 15 cigarettes / day	1784	4.6	1337	3.4	484	2.5
Smoke 15 + cigarettes / day	1832	4.7	1301	3.3	351	1.8

Table 3.7 (continued)

100K Paper Comparative Analysis: Age at Screening
Data as of: 2/28/97

Variable	50 - 59 (n=39366) n	%	60 - 69 (n=39814) n	%	70 - 79 (n=19525) n	%
Alcohol**						
Non drinker	3424	8.8	4208	10.6	2563	13.2
Past drinker	6834	17.5	7221	18.3	4009	20.7
Drink < 1 beverage / mo	5318	13.6	4829	12.2	2075	10.7
Drink < 1 beverage / wk	8245	21.1	8135	20.6	3855	19.9
Drink 1 - < 7 beverages / wk	10958	28.0	10194	25.8	4568	23.6
Drink 7 + drinks / wk	4341	11.1	4944	12.5	2282	11.8
Moderate or Strenuous Activity[8,**]**						
No activity	7278	20.1	7043	19.1	3550	19.3
Some activity	12443	34.4	13264	36.0	7100	38.7
2 - 4 episodes per week	6444	17.8	6607	17.9	3329	18.1
4 + episodes per week	9995	27.6	9946	27.0	4384	23.9
Use of Supplements**	25018	63.6	27105	68.1	13972	71.6
Depression[6,**]**	5322	13.8	3844	9.9	1605	8.5

OS women only

	50 - 59 (n=20698) n	%	60 - 69 (n=22108) n	%	70 - 79 (n=12387) n	%
Cancer Ever[3,4,12**]**	1966	9.6	2652	12.2	1964	16.1
Breast Cancer Ever[12,**]**	840	4.1	1131	5.1	796	6.4
Colon Cancer Ever[6,12,**]**	67	0.3	174	0.8	204	1.7
Endometrial Cancer Ever[7,12**]**	275	1.3	379	1.7	335	2.7
Cervical Cancer Ever[3,12]**	271	1.4	248	1.2	143	1.3
Ovarian Cancer Ever[3,12**]**	109	0.6	139	0.7	101	0.9
Melanoma Cancer Ever[3,12,**]**	255	1.2	392	1.8	311	2.5

[1] Shown for Form 2 Versions 2 and 3 only (n=94586)
[2] Shown for Form 30, version 3 only (n=91294)
[3] Shown for Form 30, version 2 and 3 only (n=95669)
[4] Excluding nonmelanoma skin cancer
[5] Defined as a score of .06 or greater from the shortened CESD/DIS algorithm.
[6] CT: Applies only HRT participants who had colon cancer > 10 years ago. OS: Applies to all participants
[7] CT: Applies to only DM participants who had endometrial cancer > 10 years ago. OS: Applies to all participants
[8] Episodes defined as 20+ minutes of continuous activity. Shown for Form 34 Version 2 only (n=91562)
[9] Shown only for OS participants.
[10] Applies only participants 55 and older.
[11] 'Other' ethnicity comprised of American Indians (n=419), Asians (n=2363), and Other / Unspecified (n=1224)
[12] Applies to OS participants only.
** Indicates significant association with ethnicity at the .01 level from Chi-squared test.

Table 3.7 (continued)

100K Paper Comparative Analysis: Age at Screening
Data as of: 2/28/97

Variable	50 - 59 (n=39366) N	Mean	SD	60 - 69 (n=39814) N	Mean	SD	70 - 79 (n=19525) N	Mean	SD
Blood Pressure (mm Hg)									
Systolic**	39332	121.3	15.9	39775	128.3	17.4	19487	134.4	18.6
Diastolic**	39336	75.9	9.1	39772	75.3	9.2	19495	73.7	9.6
BMI (kg/m^2)**	39099	28.1	6.2	39537	28.0	5.9	19383	27.0	5.2
Waist (cm)**	39229	85.8	14.4	39667	86.8	13.7	19458	85.6	12.7
WHR**	39193	0.80	0.08	39627	0.81	0.08	19440	0.82	0.08
Energy (kcal./day)**	37540	1651	594.0	38224	1590	561.8	18715	1525	543.6
Calories from fat (%)**	37540	33.7	8.6	38224	33.3	8.5	18715	32.7	8.5
Polyunsaturated Fat (%)	37540	6.8	2.4	38224	6.8	2.4	18715	6.7	2.4
Monosaturated Fat (%)**	37540	12.5	3.5	38224	12.4	3.5	18715	12.1	3.4
Saturated Fat (%)**	37540	11.8	3.5	38224	11.5	3.5	18715	11.3	3.5
Cholesterol (mg)**	37540	223.9	126.6	38224	213.5	118.8	18715	198.9	113.0
Dietary Calcium (mg)	37540	744.0	396.3	38224	740.6	396.0	18715	741.6	408.8
Vitamin D (mcg)**	37540	4.4	2.9	38224	4.6	2.9	18715	4.8	3.1
Vitamin E (mg)**	37540	7.5	3.7	38224	7.6	3.9	18715	7.5	3.8
Fiber (g)**	37540	14.4	6.0	38224	14.7	6.0	18715	14.9	6.1
Fruits and Vegetables (servings/day)**	37433	3.8	2.1	38143	4.1	2.1	18685	4.4	2.2
Typical Sleep (hrs/night)**	39157	6.8	1.0	39595	6.9	1.0	19391	6.9	1.0

** Indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.8

100K Paper Comparative Analysis: Age at Screening for DM Randomized Participants
Data as of: 2/28/97

Variable	50 - 59 (n = 14489) N	Mean	SD	60 - 69 (n = 13130) N	Mean	SD	70 - 79 (n = 4778) N	Mean	SD
Blood Pressure (mm Hg)									
Systolic**	14488	122.6	15.9	13128	129.2	17.0	4778	135.0	18.3
Diastolic**	14489	76.6	9.0	13125	75.8	9.0	4774	74.0	9.4
BMI (kg/m^2)**	14432	29.0	6.0	13090	29.1	5.7	4763	28.2	5.2
Waist (cm)**	14451	88.1	14.0	13100	89.4	13.5	4769	88.3	12.7
WHR**	14440	0.80	0.08	13092	0.82	0.08	4768	0.83	0.08
Energy (kcal./day)**	13996	1780	616.3	12800	1716	589.7	4692	1642	578.9
Calories from fat (%)**	13996	38.9	5.0	12800	38.8	4.9	4692	38.4	4.7
Polyunsaturated Fat (%)	13996	7.8	2.2	12800	7.9	2.2	4692	7.9	2.2
Monosaturated Fat (%)**	13996	14.5	2.2	12800	14.5	2.1	4692	14.3	2.1
Saturated Fat (%)**	13996	13.7	2.6	12800	13.5	2.6	4692	13.4	2.6
Cholesterol (mg)**	13996	260.7	125.5	12800	251.1	120.6	4692	237.3	117.9
Dietary Calcium (mg)	13996	726.7	372.1	12800	721.9	365.4	4692	721.4	379.8
Vitamin D (mcg)**	13996	4.5	2.7	12800	4.7	2.8	4692	4.9	2.8
Vitamin E (mg)	13996	8.4	3.7	12800	8.4	3.9	4692	8.3	3.9
Fiber (g)**	13996	13.6	5.3	12800	13.8	5.4	4692	14.0	5.5
Fruits and Vegetables (servings/day)**	13928	3.3	1.7	12752	3.6	1.8	4675	3.9	1.8

** Indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.9

100K Paper Comparative Analysis: Age at Screening for HRT Randomized Participants
Data as of: 2/28/97

Variable	50 - 59 (n = 6467) N	Mean	SD	60 - 69 (n = 6762) N	Mean	SD	70 - 79 (n = 3127) N	Mean	SD
Blood Pressure (mm Hg)									
Systolic**	6467	122.9	16.0	6762	129.5	17.2	3127	135.3	18.7
Diastolic**	6467	77.0	9.0	6762	76.0	9.0	3126	74.2	9.4
BMI (kg/m^2)**	6442	29.5	6.3	6732	29.1	5.8	3112	27.8	5.1
Waist (cm)**	6450	89.5	14.5	6739	89.7	13.6	3119	87.7	12.6
WHR**	6442	0.82	0.09	6732	0.83	0.08	3114	0.83	0.08
Energy (kcal/day)**	6061	1666	619.7	6414	1599	574.6	2976	1538	551.8
Calories from fat (%)**	6061	34.9	8.6	6414	34.2	8.6	2976	33.1	8.4
Polyunsaturated Fat (%)**	6061	6.9	2.4	6414	6.8	2.4	2976	6.7	2.3
Monosaturated Fat (%)**	6061	13.1	3.5	6414	12.8	3.5	2976	12.3	3.4
Saturated Fat (%)**	6061	12.2	3.5	6414	11.9	3.5	2976	11.5	3.4
Cholesterol (mg)**	6061	236.9	132.4	6414	222.9	124.3	2976	204.3	115.7
Dietary Calcium (mg)	6061	720.8	396.1	6414	732.7	397.0	2976	737.9	397.2
Vitamin D (mcg)**	6061	4.3	2.9	6414	4.6	2.9	2976	4.8	3.0
Vitamin E (mg)	6061	7.4	3.6	6414	7.5	3.8	2976	7.5	3.9
Fiber (g)**	6061	13.8	6.0	6414	14.2	5.8	2976	14.8	6.0
Fruits and Vegetables (servings/day)**	6030	3.5	2.1	6386	3.9	2.0	2972	4.3	2.2

** Indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.10

100K Paper Comparative Analysis: Age at Screening for Clinical Trial Participants
Data as of: 2/28/97

Variable	50 - 59 (n = 18638) N	Mean	SD	60 - 69 (n = 17679) N	Mean	SD	70 - 79 (n = 7110) N	Mean	SD
Blood Pressure (mm Hg)									
Systolic**	18637	122.5	15.9	17677	129.2	17.1	7110	135.0	18.5
Diastolic**	18638	76.6	9.0	17674	75.8	9.0	7106	74.1	9.4
BMI (kg/m^2)**	18561	29.0	6.1	17620	28.9	5.7	7083	27.9	5.1
Waist (cm)**	18591	88.1	14.1	17632	89.1	13.5	7094	87.9	12.6
WHR**	18574	0.81	0.08	17619	0.82	0.08	7089	0.83	0.08
Energy (kcal/day)**	17858	1741	617.6	17074	1672	585.5	6891	1597	568.7
Calories from fat (%)**	17858	37.5	6.7	17074	37.0	6.9	6891	36.1	7.1
Polyunsaturated Fat (%)**	17858	7.5	2.3	17074	7.5	2.3	6891	7.4	2.4
Monosaturated Fat (%)**	17858	14.0	2.8	17074	13.8	2.8	6891	13.4	2.9
Saturated Fat (%)**	17858	13.1	3.0	17074	12.9	3.0	6891	12.6	3.1
Cholesterol (mg)**	17858	251.7	127.8	17074	239.1	121.2	6891	222.3	117.5
Dietary Calcium (mg)	17858	726.4	379.0	17074	727.1	377.8	6891	728.7	387.5
Vitamin D (mcg)**	17858	4.4	2.8	17074	4.7	2.8	6891	4.8	2.9
Vitamin E (mg)	17858	8.1	3.7	17074	8.1	3.9	6891	8.0	3.9
Fiber (g)**	17858	13.7	5.6	17074	14.0	5.6	6891	14.3	5.7
Fruits and Vegetables (servings/day)**	17776	3.4	1.8	17009	3.7	1.9	6873	4.1	2.0

** Indicates significant association with ethnicity at the .01 level from ANOVA model.

Table 3.11

100K Paper Comparative Analysis: Ethnicity by Age at Screening by Education, Income
Data as of: 2/28/97

Ethnicity*Age at Screening*Education[1,3]

	White		Black		Hispanic		Other	
	n	%	n	%	n	%	n	%
50 - 59								
0-8 years	100	0.3	59	1.5	366	19.9	21	1.3
Some high school	503	1.6	256	6.3	156	8.5	37	2.3
High School Diploma / GED	4265	13.5	514	12.7	284	15.5	153	9.4
School after high school	11537	36.6	1717	42.4	629	34.2	605	37.0
College degree or higher	15091	47.9	1506	37.2	403	21.9	820	50.1
60 - 69								
0-8 years	224	0.7	120	3.7	245	21.0	31	2.0
Some high school	983	2.9	349	10.9	121	10.4	57	3.8
High School Diploma / GED	6583	19.6	461	14.3	194	16.6	276	18.2
School after high school	12562	37.4	1185	36.8	366	31.3	578	38.1
College degree or higher	13278	39.5	1101	34.2	242	20.7	574	37.9
70 - 79								
0-8 years	194	1.1	98	8.2	70	22.7	53	6.5
Some high school	673	3.9	162	13.5	40	12.9	70	8.6
High School Diploma / GED	3168	18.6	164	13.7	39	12.6	181	22.1
School after high school	6888	40.4	376	31.3	111	35.9	300	36.7
College degree or higher	6137	36.0	401	33.4	49	15.9	214	26.2

Ethnicity*Age at Screening*Family Income[2,3]

	White		Black		Hispanic		Other	
	n	%	n	%	n	%	n	%
50 - 59								
< $10,000	638	2.1	335	8.7	328	19.5	58	3.7
$10,000-$19,999	1629	5.4	484	12.6	305	18.2	95	6.1
$20,000-$34,999	4862	16.1	890	23.2	323	19.2	260	16.6
$35,000-$49,999	5892	19.5	756	19.7	282	16.8	251	16.0
$50,000-$74,999	7776	25.7	813	21.2	250	14.9	398	25.4
$75,000 +	9409	31.1	559	14.6	192	11.4	507	32.3
60 - 69								
< $10,000	964	3.0	490	16.3	222	21.3	77	5.4
$10,000-$19,999	3883	12.3	635	21.2	243	23.3	194	13.6
$20,000-$34,999	8916	28.2	733	24.4	248	23.8	310	21.8
$35,000-$49,999	7266	23.0	499	16.6	163	15.7	312	21.9
$50,000-$74,999	5910	18.7	428	14.3	103	9.9	292	20.5
$75,000 +	4716	14.9	215	7.2	62	6.0	239	16.8
70 - 79								
< $10,000	800	5.0	256	23.8	66	23.9	48	6.5
$10,000-$19,999	3242	20.4	307	28.5	79	28.6	168	22.6
$20,000-$34,999	5186	32.6	262	24.3	73	26.4	235	31.6
$35,000-$49,999	3164	19.9	133	12.3	35	12.7	137	18.4
$50,000-$74,999	2173	13.6	91	8.4	18	6.5	102	13.7
$75,000 +	1358	8.5	28	2.6	5	1.8	53	7.1

[1] Indicates a significant association between education and age at screening*ethnicity interaction effect at the .001 level from the following ANOVA model:
E(Education) = Age + ethnicity + Age*ethnicity + Error.

[2] Indicates a significant association between income and age at screening*ethnicity interaction effect at the .001 level from the following ANOVA model:
E(Income) = Age + ethnicity + Age*ethnicity + Error.

[3] Note that model assume a linear response variable.

Table 3.11 (continued)

100K Paper Comparative Analysis: Ethnicity by Age by Depression
Data as of: 2/28/97

Ethnicity*Age at Screening*Depression

	White		Black		Hispanic		Other	
	n	%	n	%	n	%	n	%
50 - 59								
No	27161	86.9	3292	83.9	1305	77.8	1403	86.8
Yes	4102	13.1	633	16.1	373	22.2	214	13.2
60 - 69								
No	30065	90.7	2674	86.6	870	81.6	1351	91.1
Yes	3101	9.4	415	13.4	196	18.4	132	8.9
70 - 79								
No	15333	91.9	990	87.8	225	80.9	722	91.2
Yes	1344	8.1	138	12.2	53	19.1	70	8.8

4. HRT Intervention Status

4.1 Adherence

Women randomized to HRT are required to come for a clinic visit six and twelve months after randomization and annually thereafter. Adherence to medications is determined at visits by weighing returned bottles if available or by self-report in a small proportion of cases. Symptoms and outcomes are also ascertained at these visits. Telephone contacts are also required at 6 weeks and on the anniversary of their six month visits. These contacts serve mostly to assure safety, ascertain outcomes and promote bonding. Adherence data from these contacts are limited so we do not report them here.

Table 4.1 - HRT Adherence Summary gives descriptive data on all women who are considered due for each contact by treatment arm. Rates of visits conducted, visits within window, stopping intervention and taking assigned medications are shown by treatment arm for each interval for which we have adherence data. Note that for stopping intervention and medication rates we have excluded the 331 who were moved from ERT to PERT in early 1995 after our protocol change. A large proportion of these women (34%) have stopped intervention. Since their experience is unique in the trial, including their results here would skew these data away from what would be expected in the remaining women. The final column is the adherence summary presenting the proportion of women known to have consumed more than 80% of their assigned HRT pills during that interval. Differences between women with and without an intact uterus are small and do not show clear trends over time.

Table 4.2 presents estimated drop-in and drop-out rates based on observed data and the associated design assumptions. The design assumptions underestimated the observed values to date, particularly the first two years of follow-up. The power calculations assumed that 6% of HRT women would stop intervention in the first year with an additional 3% per year thereafter. An independent assumption of 3% per year lost to follow-up or competing risk events gives an overall drop-out rate of 8.8% in year 1, and 5.9% per year thereafter. Our lifetable estimate of the AV-1 drop-out rate is 9.6%, and our estimate for drop-out between AV-1 and AV-2 is 10.0% with small differences between those women with and without a uterus.

The power calculations also assumed that a small proportion (1.5% per year) of the HRT participants randomized to placebo would begin taking hormones outside of the trial. Among hysterectomized women this observed rate is roughly 3% per year; in women with a uterus it averages 1.7% per year.

Adherence to HRT was not explicitly modeled in the power calculations with the exception of stopping the intervention entirely or changing from placebo to active. Adherence is incorporated implicitly, though, through the selection of treatment effect size as these values were gleaned from population based studies of hormones and disease incidence. To the extent that the WHI adherence pattern mimics hormone use in post-menopausal women generally, study power will be preserved. We expect that our adherence rates are somewhat better than those of women prescribed hormones

by their personal physician. Berman, et al (1996)[1] reports a stopping ERT rate of 20% at 6 months (with or without progesterone), 38% at 1 year, 51% at 18 months and 59% at 2 years in a study population of 2106 women, aged 46-63, enrolled in a prescription reimbursement plan in Minnesota. Adherence, defined as taking 80% or more pills during the interval since initial prescription was estimated to be 68% at 2 months, 37% at 6 months, 24% at one year and 10% at 2 years. In a 1995 review of 42 studies, Udoff et al[2] displayed ranges for stopping combined continuous HRT of 11%-33% at 6 months, 8%-40% at 1 year and 12-24% at 2 years. This suggests that our experience meets or exceeds the adherence rates in the general population. Nevertheless, the observed level of adherence may not be sufficient, however, if the desired effect is tied to recent or current use.

The effects on power of somewhat greater drop-out rates are shown in *Table 4.3*. Revised calculations assuming 7% drop-outs in years 1 and 2 and 4% per year through the remaining follow-up (independent of the 3% loss to follow-up rates) and 2.5% drop-ins per year throughout follow-up produced a power for the ERT vs. Placebo comparison on CHD rates of 71% compared to the design value of 81%. For the PERT comparison the power drops from 88% to 80%. The powers for hip fractures and breast cancer comparisons are similarly reduced.

Subsequent tables examine HRT adherence in relation to study subject and program characteristics. The summary adherence measure mentioned above was used in these analyses. Specifically, a binary variable was defined for each HRT participant that described whether (binary variable equal one) or not (binary variable equal zero) she reported taking 80% or more of her HRT pills in the preceding time interval (randomization to SAV-1, SAV-1 to AV-1, or AV-1 to AV-2). The odds ratio for this binary event was then associated jointly with selected study subject and program characteristics, using logistic regression techniques. Similar analyses were also carried out for the binary variable that specifies whether or not a stopped medication (Form 7) was filed. For brevity, and since the criteria for filing Form 7 apparently vary considerably among CC's, these analyses are not included.

Table 4.4 shows numbers of HRT women, summary adherence odds ratios (OR), separately by baseline uterine status for the time period up to SAV-1 as a function of various factors. Among women with a uterus, note the lesser adherence among women reporting bleeding at 6 weeks from randomization, and the much improved adherence (OR=2.65) among women receiving the six week phone call. Adherence among these women is somewhat better among women having greater education or higher family income, is slightly poorer if randomized in the DM component of the Clinical Trial, and is noticeably poorer if the woman is of racial/ethnic minority status. Among hysterectomized women, the 6 week phone call is associated with better adherence and minority status with poorer adherence.

Table 4.5 examines adherence in the time period SAV-1 to AV-1 in relation to these and other factors, among women who reported taking 80% or more of their pills up to SAV-1. Given that a

[1] Berman RS et al (1996). Compliance of Women in Taking Estrogen Replacement Therapy. Journal of Women's Health 5(3):213-220.

[2] Udoff L, Langerberg P and Adash EY (1995). Combined Continuous Hormone Replacement Therapy: A Critical Review. Obstetrics & Gynecology 86(2):306-316.

woman was adherent to medication during the first six-month period, her bleeding pattern (among women with a uterus) within that first six months was not strongly related to adherence in the subsequent six months, as was also the case for the six-week phone call. Hence these factors seem important primarily in the first few months from randomization. Note that the relatively small fraction of women who underwent HRT washout prior to randomization have better adherence between SAV-1 and AV-1, perhaps because of a longer history of HRT pill taking, and that minority women become newly non-adherent between SAV-1 and AV-1 at a comparatively higher rate.

Table 4.6 considers medication adherence between AV-1 and AV-2 among women who reported taking 80% or more of their HRT pills at AV-1. The data are now considerably more sparse. However, it appears as though women who report bleeding at AV-1 may be at increased risk for non-adherence between AV-1 and AV-2 (though not significant at present). Among hysterectomized women, one can note that younger women (ages 50-54) are at elevated risk for new non-adherence between AV-1 and AV-2.

Baseline psychosocial variables (Form 37) were also examined in relation to medication adherence up to SAV-1 and between SAV-1 and AV-1 and psychosocial variables at AV-1 (Form 38) were examined in relation to adherence between AV-1 and AV-2. For brevity only selected odds ratios from these analyses are given in *Table 4.7*. These analyses also include the factors listed in Table 4 as control variables. The left side of *Table 4.7* lists psychosocial variable constructs, along with a small number of individual questionnaire items and identifies the Form 37/38 questions from which these variables are constructed. (For descriptions of the psychosocial behavioral constructs, see Appendix A.) The odds ratios shown correspond to a 0.5 standard deviation upward shift in the listed variable. All variables were defined so that larger values represent a more favorable state than smaller values, by reversing the sign of the variable (as indicated on table) if necessary.

Even though the odds ratios in *Table 4.7* tend to be close to unity (in part because they reflect shift of only 0.5 standard deviation) it is impressive that virtually all odds ratios in the anticipated direction (i.e. greater than unity) and that many are significantly greater than unity. This also tended to be true for the responses to other individual Form 37/38 questions (not shown). The general interpretation of these analyses seems clear: women with few health or emotional limitations or symptoms, and women who are satisfied with their lives and have a supportive environment tend to adhere a little better to their HRT medications. The same patterns tend to hold for adherence up to SAV-1 and between SAV-1 and AV-1 in relation to baseline psychosocial measures and for adherence between AV-1 and AV-2 in relation to psychosocial measures at AV-1. As in previous tables adherence analyses for SAV-1 to AV-1, were based on women consuming 80% or more of their pills at SAV-1 and adherence analysis for SAV-1 to AV-2 were based on women consuming 80% or more of their pills at AV-1.

A number of additional factors were also examined in relation to HRT adherence. These include From 2/3 (Eligible Screen) variables related to the form of first WHI contact (mailed letter, friend/relative,...), and the woman's initial expression of interest in HRT; Form 20 (Personal Information) variables related to use of medical care and previous medical procedures; From 30 (Medical History) variables related to hospitalization and health conditions; Form 31 (Reproductive

History) variables related to age at menopause, menopausal symptoms, and breast biopsies; Form 32 (Family History) variables related to selected vascular diseases, cancers and fractures; Form 34 (Personal Habits) variables related to smoking and diet; Form 80 (Physical Measurement) variables; Form 85 (Mammogram); and Form 100 (Blood Counts). In general there was little relationship between these factors and HRT adherence, so that detailed analyses are not listed here. It can be commented that women with a uterus who had a breast biopsy were somewhat less likely to be adherent (odds ratio 0.8 between baseline and SAV-1, and 0.7 between SAV-1 and AV-1; both significant) as was also the case among women who reported breast cancer in a female relative (odds ratio 0.8 between baseline and SAV-1, and 0.8 between SAV-1 and AV-1, the latter significant). These associations were, however, not apparent among hysterectomized women.

Table 4.8 - Reasons for Stopping HRT summarizes the frequency of reported reasons for stopping interventions by hysterectomy status.

4.2 Symptoms

Women may report symptoms potentially related to HRT at routine follow-up contacts or through non-routine contacts with the CC. The primary symptoms being monitored are bleeding and breast changes. Reports of bleeding and breast changes by contact type are shown in *Tables 4.9* and *4.10*, respectively. As expected there are clear differences between active and placebo arms though these differences diminish over time.

4.3 Safety Monitoring

Table 4.11 - Results of Endometrial Monitoring presents results of endometrial aspirations by time since randomization and study arm. As routine post-randomization biopsies are required of only a small sample (6%) of women at AV-3, AV-6, and AV-9, the vast majority of these tests represent non-routine aspirations performed to address bleeding problems. Among 913 biopsies, 36 (3.9%) yielded an abnormal result: 24 cystic, 5 adenomatous, 5 atypia and 2 cancer.

4.4 Issues

While HRT adherence rates in the WHI appear to be impressive relative to adherence rates in routine clinical practice, they fall somewhat short of CT design assumptions, particularly following AV-1. WHI adherence data can help identify program activities that may help to enhance adherence, and can help identify subsets of women who may need additional support and assistance to remain adherent.

Improving adherence to the HRT regimen is a high priority of the WHI program. To address adherence problems associated with bleeding, we have modified the protocol to allow additional flexibility for the local gynecologists to use additional, open-label medroxyprogesterone (MPA 2.5 or 5 mg) or open-label conjugated equine estrogen (CEE 0.3 mg) as an option for short-term treatment for bleeding after the first 6 months.

Other sources of adherence problems appear to be related to external pressure from primary care providers to be on active hormones and the need for more support and reassurance from clinics to stay on blinded medications in the face of conflicting information and non-specific symptoms.

An HRT Adherence Summit was convened in May 1997 to review analysis of factors associated with adherence, to identify strategies to improve adherence and to develop a plan to implement these. Multivariate analyses similar to those shown above examined the relationship between psychosocial factors assessed at baseline and subsequent adherence. These analysis confirmed our general intuition that better mental health and social support were associated with better adherence. The effect of the 6-week phone call in improving adherence also suggests that more attention from clinic staff can help. The challenge, of course, is to accomplish this within the existing resources. Those in attendance generated ideas for participant and clinic level tasks that should be considered for their potential to increase adherence without substantial increases in costs. When complete, these suggestions will be provided to CCs in the form of a "Hot Tips" booklet.

The PMC is also focusing on adherence problems. They have conducted site visits specifically for CCs having poorer than average adherence. To become more pro-active, the PMC will be visiting sites with the best adherence to learn about their systems and efforts to track and manage adherence problems. A model for managing adherence will be developed from these examples and offered to a few clinics having difficulties as a test of the model. When feedback has been received and incorporated, the model will be provided to all CCs for their use.

Table 4.1
HRT Adherence Summary

	Due	Conducted		Conducted in Window		Stopped HRT during interval		Missed Pill Collection		Total with Collections		Medication Rate[1] <50%		Medication Rate[1] 50%-80%		Medication Rate[1] 80% +		Adherence Summary[2]
	N	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	%
6 Week	18761	17609	94	14558	78													
Semi-Annual Visit-1	15973	15465	97	12974	81	772	4.9	1171	8	14457	93	510	4	1074	7	12873	89	82
With Uterus	9638	9371	97	7940	82	471	5.1	631	7	8673	93	315	4	589	7	7769	90	84
Without Uterus	6335	6094	96	5034	79	301	4.8	540	9	5784	92	195	3	485	8	5104	88	81
Annual Visit-1	11300	10754	95	8706	77	533	4.9	762	7	9474	93	438	5	886	9	8150	86	75
With Uterus	6784	6483	96	5248	77	294	4.6	440	7	5594	93	257	5	468	8	4869	87	76
Without Uterus	4516	4271	95	3458	77	239	5.3	322	8	3880	92	181	5	418	11	3281	85	73
Annual Visit-2	4807	4480	93	3513	73	444	10.0	437	11	3425	89	122	4	378	11	2925	85	66
With Uterus	2842	2675	94	2117	74	216	8.6	218	10	1962	90	71	4	194	10	1697	87	68
Without Uterus	1965	1805	92	1396	71	228	11.7	219	13	1463	87	51	4	184	13	1228	84	63
Annual Visit -3	1304	1175	90	951	73	53	4.7	83	10	782	90	39	5	73	9	670	86	60
With Uterus	759	692	91	552	73	24	4.1	51	11	409	89	19	5	39	10	351	86	60
Without Uterus	545	483	89	399	73	29	5.4	32	8	373	92	20	5	34	9	319	86	59

[1] Medication rate calculated as number of pills taken divided by number of days since bottle(s) were dispensed.

[2] Adherence summary calculated as number of women consuming ≥ 80% of pills / # due for visit.

Note: Deceased women are excluded from all medication adherence calculations.

Table 4.2
HRT Drop-Out and Drop-In Rates (%) by Follow-Up Time
(Design-specified values in parentheses)

	Without Uterus		With Uterus		Overall Total	
	Interval[1]	Cumulative[2]	Interval	Cumulative	Interval	Cumulative
Drop-Outs[3]						
AV-1	9.8 (8.8)	9.8 (8.8)	9.5 (8.8)	9.5 (8.8)	9.6 (8.8)	9.6 (8.8)
AV-2	11.7 (5.9)	20.3 (14.2)	8.6 (5.9)	17.3 (5.9)	10.0 (5.9)	18.6 (14.2)
AV-3	5.4 (5.9)	24.6 (19.2)	4.1 (5.9)	20.7 (19.1)	4.7 (5.9)	22.5 (19.2)
Drop-Ins[4]						
AV-1	2.9 (1.5)	2.9 (1.5)	2.0 (1.5)	2.0 (1.5)	2.4 (1.5)	2.4 (1.5)
AV-3	2.8 (2.9)	5.6 (4.4)	3.4 (2.9)	5.3 (4.4)	3.1 (2.9)	5.4 (4.4)

[1] Estimates of stopping or starting hormones in the Interval

[2] Estimates of cumulative rates

[3] Drop-out rates derived from Form 7 by date. Cumulative rates calculated as life-table estimates.

[4] Cumulative Drop-in rates derived from medication inventory collected at AV-1, AV-3, AV-6, AV-9. Interval estimates back-calculated from cumulative rates.

Table 4.3
Sensitivity of HRT Study Power to Adherence Assumptions

Outcome	Year	Intervention Effect[1] (%)	Percentage of Cases		Power			
					ERT vs. Placebo		PERT vs. Placebo	
			Control	Intervention	Design[1]	Revised Adherence Rates[2]	Design[1]	Revised Adherence Rates[2]
CHD	2001	25	3.26	2.71	46	40	54	47
		30	3.26	2.60	62	54	70	63
		35	3.25	2.49	76	68	84	77
	2004	25	5.03	4.16	64	55	73	63
		30	5.02	3.97	[81][3]	71	[88]	80
		35	5.01	3.79	92	85	96	91
Hip Fractures	2001	25	1.88	1.55	31	27	37	32
		30	1.87	1.49	43	37	51	44
		35	1.87	1.42	56	49	65	57
	2004	25	3.14	2.58	48	40	56	47
		30	3.13	2.46	[65]	54	[73]	63
		35	3.12	2.35	79	69	86	77
Breast Cancer	2001	15	2.07	2.25	12	10	13	12
		22	2.08	2.35	21	18	24	21
	2004	15	3.04	3.40	24	20	29	24
		22	3.05	3.60	46	38	54	45
	2009	15	4.53	5.21	47	36	55	43
		22	4.56	5.58	[79]	66	[87]	75

[1] Drop-out rates of 6% in year 1, 3% per year thereafter; Drop-in rate of 1.5% per year.

[2] Drop-out rates of 7% in years 1 and 2, 4% thereafter; Drop-in rate of 2.5% per year.

[3] Design values

Table 4.4
Logistic Regression Analysis of HRT Medication Adherence between Baseline and Semi-annual Visit (SAV-1)[1]

	HRT (n=15628)					
	With Uterus (n=9304)			Without Uterus (n=6324)		
	Non-Adherent Participants (n=1535)	Adherent Participants[2] (n=7769)	OR for adherence (>80%)[3]	Non-Adherent Participants (n=1220)	Adherent Participants[2] (n=5104)	OR for adherence (>80%)[3]
Age:						
50-54	277	1325	1.00	252	916	1.00
55-59	355	1825	1.06	263	995	1.02
60-69	575	3274	1.10	450	2133	1.18
70-79	328	1345	0.78*	255	1060	1.00
Ethnicity:						
White	1160	6681	1.00	764	3952	1.00
Black	147	483	0.62**	284	715	0.51**
Hispanic	165	340	0.53**	133	265	0.45**
Other Minority	58	244	0.78	37	162	0.84
Education:						
0-8 Yrs	84	134	1.00	56	144	1.00
Some H.S./Diploma	389	1747	1.56*	351	1444	0.91
Post H.S.	1052	5841	1.82**	796	3474	0.98
Income:						
<20K	429	1647	1.00	409	1495	1.00
20-35K	390	2051	1.15	309	1424	1.05
35-50K	272	1564	1.19	217	945	0.98
>50K	397	2360	1.21*	246	1123	1.00
DM Randomized:						
No	1029	5406	1.00	797	3319	1.00
Yes	506	2363	0.89	423	1785	1.07
HRT Washout:						
No	1435	7148	1.00	1064	4382	1.00
Yes	100	621	1.20	156	722	1.11
Marital Status:						
Married	860	4629	1.00	630	2860	1.00
Not Married	663	3115	1.00	579	2218	0.92
Hormones Ever:						
No	917	4549	1.00	479	1955	1.00
Yes	618	3220	1.01	741	3149	0.93

Table 4.4 (continued)

	HRT (n=15628)					
	With Uterus (n=9304)			Without Uterus (n=6324)		
	Non-Adherent Participants (n=1535)	Adherent Participants[2] (n=7769)	OR for adherence (>80%)[3]	Non-Adherent Participants (n=1220)	Adherent Participants[2] (n=5104)	OR for adherence (>80%)[3]
6 wk phone call						
No	207	386	1.00	152	349	1.00
Yes	1328	7383	2.65**	1068	4755	1.62**
On-Study Bleeding						
No bleeding reported at 6wks	1153	5970	1.00			
Bleeding reported at 6wks	357	1747	0.82*			

[1] Excludes ERT to PERT participants.

[2] Adherence defined as participants who took at least 80% of HRT medications. If a participant does not have a pill collection, then her adherence estimate equals 0.

[3] Assuming asymptotic normality for parameter estimates.

* P-value <=.05 from Wald test.

** P-value <=.01 from Wald test.

Table 4.5

Logistic Regression Analysis of HRT Medication Adherence between Semi-annual Visit 1 (SAV1) and Annual Visit 1 (AV1) for those Participants with 80% Medication Adherence at Semi-annual Visit 1 (SAV1)[1]

	HRT (n=9063)					
	With Uterus (n=5414)			Without Uterus (n=3649)		
	Non-Adherent Participants (n=788)	Adherent Participants[2] (n=4626)	OR for adherence (>80%)[3]	Non-Adherent Participants (n=566)	Adherent Participants[2] (n=3083)	OR for adherence (>80%)[3]
Age:						
50-54	134	835	1.00	117	581	1.00
55-59	188	1134	0.93	120	614	1.04
60-69	333	1927	0.88	241	1263	1.06
70-79	133	730	0.91	88	625	1.51*
Ethnicity:						
White	639	4038	1.00	389	2438	1.00
Black	73	261	0.57**	112	406	0.60**
Hispanic	45	182	0.74	46	144	0.62*
Other Minority	30	134	0.73	18	89	0.81
Education:						
0-8 Yrs	18	73	1.00	23	87	1.00
Some H.S./Diploma	177	1010	1.03	155	854	0.94
Post H.S.	586	3521	1.13	383	2112	0.94
Income:						
<20K	190	950	1.00	172	876	1.00
20-35K	195	1238	1.11	179	886	0.85
35-50K	152	947	1.05	89	585	1.20
>50K	235	1410	0.92	108	674	1.12
DM Randomized:						
No	551	3167	1.00	374	1967	1.00
Yes	237	1459	1.04	192	1116	1.18
HRT Washout:						
No	748	4230	1.00	507	2637	1.00
Yes	40	396	1.82**	59	446	1.60*
Marital Status:						
Married	421	2806	1.00	303	1763	1.00
Not Married	362	1811	0.76**	259	1302	0.96

Table 4.5 (continued)

	HRT (n=9063)					
	With Uterus (n=5414)			Without Uterus (n=3649)		
	Non-Adherent Participants (n=788)	Adherent Participants[2] (n=4626)	OR for adherence (>80%)[3]	Non-Adherent Participants (n=566)	Adherent Participants[2] (n=3083)	OR for adherence (>80%)[3]
Hormones Ever:						
No	450	2684	1.00	212	1189	1.00
Yes	338	1942	0.87	354	1894	0.83
6 Wk Phone Call:						
No	49	239	1.00	52	223	1.00
Yes	739	4387	1.04	514	2860	1.07
Reported Breast Changes at 6 Months:						
No	718	4340	1.00	532	2909	1.00
Yes	57	254	0.81	32	153	0.84
On-Study Bleeding:						
No Bleeding	499	3101	1.00			
Bleeding at 6 Weeks Only	28	161	0.98			
Bleeding at 6 Months Only	81	398	0.81			
Bleeding Reported at 6 Weeks *and* 6 Months	163	901	0.86			

[1] Excludes ERT to PERT participants.

[2] Adherence defined as participants who took at least 80% of HRT medications. If a participant does not have a pill collection, then her adherence estimate equals 0.

[3] Assuming asymptotic normality for parameter estimates.

* P-value <=.05 from Wald test.

** P-value <=.01 from Wald test.

Table 4.6

Logistic Regression Analysis of HRT Medication Adherence between Annual Visit 1 (AV1) and Annual Visit 2 (AV2) for those Participants with 80% Medication Adherence at AV1[1]

	HRT (n=3307)					
	With Uterus (n=1885)			Without Uterus (n=1422)		
	Non-Adherent Participants (n=325)	Adherent Participants[2] (n=1560)	OR for adherence (>80%)[3]	Non-Adherent Participants (n=277)	Adherent Participants[2] (n=1145)	OR for adherence (>80%)[3]
Age:						
50-54	60	252	1.00	64	186	1.00
55-59	88	371	0.92	47	206	1.57*
60-69	131	716	1.16	113	520	1.60*
70-79	46	221	1.04	53	233	1.52
Ethnicity:						
White	266	1429	1.00	216	946	1.00
Black	31	68	0.44**	43	147	0.74
Hispanic	24	28	0.25**	11	31	0.64
Other Minority	4	33	1.68	6	18	0.81
Education:						
0-8 Yrs	10	19	1.00	8	30	1.00
Some H.S./Diploma	65	369	1.35	80	331	0.76
Post H.S.	247	1169	0.95	188	776	0.81
Income:						
<20K	83	302	1.00	67	324	1.00
20-35K	92	434	1.25	84	321	0.78
35-50K	58	344	1.67*	53	223	0.87
>50K	80	461	1.62*	62	252	0.87
DM Randomized:						
No	211	975	1.00	176	689	1.00
Yes	114	585	1.11	101	456	1.18
HRT Washout:						
No	305	1461	1.00	242	1021	1.00
Yes	20	99	1.04	35	124	1.06
Marital Status:						
Married	187	972	1.00	168	669	1.00
Not Married	135	585	1.06	108	471	1.03

Table 4.6 (continued)

	HRT (n=3307)					
	With Uterus (n=1885)			Without Uterus (n=1422)		
	Non-Adherent Participants (n=325)	Adherent Participants[2] (n=1560)	OR for adherence (>80%)[3]	Non-Adherent Participants (n=277)	Adherent Participants[2] (n=1145)	OR for adherence (>80%)[3]
Hormones Ever:						
No	183	907	1.00	92	464	1.00
Yes	142	653	0.91	185	681	0.70*
6 week phone call:						
No	28	122	1.00	32	110	1.00
Yes	297	1438	1.13	245	1035	1.21
Reported Breast Changes:						
No breast changes	288	1365	1.00	242	1036	1.00
Breast changes at 6 months only	18	104	1.43	15	61	0.92
Breast changes at 1 year only	13	52	1.01	11	23	0.51
Breast changes at 6 months and 1 year	3	15	1.06	1	14	2.86
On-Study Bleeding:						
No Bleeding	205	1026	1.00			
Bleeding at 6 weeks only	10	39	0.82			
Bleeding at 6 months only	18	82	0.91			
Bleeding reported at 6 weeks and 6 months	10	28	1.50			
Bleeding reported at 1 year	18	135	0.58			
Bleeding reported at 6 weeks, 1year	5	12	0.42			
Bleeding reported at 6 months, 1 year	12	55	0.93			
Bleeding reported at 6wks,6months,1yr	39	140	0.66*			

[1] Excludes ERT to PERT participants. The following demographic variables were included in the logistic model: Age, ethnicity, education, income, DM randomized, HRT washout, marital status, hormones ever, 6 week phone call, breast changes, bleeding reported.

[2] Adherence defined as participants who took at least 80% of HRT medications. If a participant does not have a pill collection, then her adherence estimate equals 0.

[3] Assuming asymptotic normality for parameter estimates.

* P-value <=.05 from Wald test.

** P-value <=.01 from Wald test.

Table 4.7
Psychosocial Predictors of Adherence to HRT

Baseline (Form 37) and Year 1 (Form 38) psychosocial variables in relation to HRT adherence in selected time periods. Adherence analyses for SAV-1to AV-1 are based on women who reported taking 80% or more of their pills at SAV-1, and adherence analyses for AV-1 to AV-2 are based on women who reported taking 80% or more of their pills at AV-1. Each entry in the odds ratio associated with an upward shift of 1 standard deviation in the psychosocial variable. An asterisk denotes statistical significance at the 0.05 level.

	Uterus Intact			Uterus Removed		
Psychosocial Behavioral Constructs[a]	Baseline to SAV-1	SAV-1 to AV-1	AV-1 to AV-2	Baseline to SAV-1	SAV-1 to AV-1	AV-1 to AV-2
(Number of Women)	(6385)	(3565)	(980)	(4481)	(2503)	(874)
Social Support Construct (Higher score indicates greater support)	1.03	1.14*		1.16*	1.02	
Social Strain Construct[b] (Higher score indicates less strain)	1.10*	1.12*		1.08	1.09	
Optimism Construct (Higher score indicates more optimism)	1.08*	1.09		1.03	1.13	
Negative Emotional Expressiveness[b] (Higher score indicates less negative expressiveness)	1.05	1.05		1.04	1.18	
Ambivalent Emotional Expressiveness[b] (Higher score indicates less ambivalence)	1.02	1.04		1.02	1.08	
Hostility Construct[b] (Higher score indicates less hostility)	1.08	1.08		1.05	1.11	
Overall Quality of Life (Form 37, Qx. 46. Higher score indicates higher perceived quality)	1.08*	1.18*	1.16*	1.09*	1.06	1.17*
Satisfaction with Quality of Life (Form 37, Qx. 47. Higher score indicates more satisfaction)	1.12*	1.16*	1.12	1.14*	1.12*	1.12
Physical Function Const. (Higher score indicates less limitations)	1.14*	1.00	1.23*	1.04	1.11	1.17*
Limitations Due to Physical Health Const. (Higher score indicates less limitations)	1.10*	1.03	1.14*	1.12*	1.10	1.20*
Limitations Due to Emotional Problems Const. (Higher score indicates less limitations)	1.12*	1.16	1.11	1.17*	1.17*	1.03
Health Interference with Social Activities (Form 37, Qx. 74. Higher score indicates less interference)	1.07*	1.09	1.11	1.12*	1.17*	1.09
Downhearted and Blue (Form 37, Qx. 80. Higher score indicates less feeling blue)	1.09*	1.16*	1.03	1.16*	1.06	1.07
Feel Worn Out (Form 37, Qx. 81. Higher score indicates less worn out)	1.16*	1.05*	1.02	1.12*	1.07	0.95
Pain Construct (Higher score indicates less pain)	1.04	1.07	1.09	1.08	0.91	1.22*
General Health Const. (Higher score indicates better health)	1.07*	1.07	1.08	1.12	1.09	1.16
Daily Living Activities Construct[b] (Higher score indicates less disability)	1.04	1.02	1.04	1.03	0.94	1.04
Overall Symptom Construct[b] (Higher score indicates fewer symptoms)	1.10*	1.12*	1.16*	1.11*	1.08	1.11
Life Event Construct[b] (Higher score indicates fewer and less upsetting life events)	1.08*	1.14*	1.04	1.15*	1.01	1.01
CES-D/DIS Depression Construct[b] (Higher score indicates less depression)	1.11*	1.10	0.91	1.10*	1.11*	1.09
Worried that sex will affect health[b] (Form 37, Qx. 124. Higher score indicates less worried)	1.08*	1.01	1.11	1.06	1.02	1.14

a - For descriptions of the psychosocial behavioral constructs, see Appendix A.

b - The sign of the parameter was reversed to reflect the description of the scoring.

Table 4.8
Reasons for Stopping HRT

Reasons[1]	With Uterus (N = 1438)	Without Uterus (N = 967)
Personal	81 (6%)	66 (7%)
Travel	27 (2%)	28 (3%)
Study Procedures	28 (2%)	14 (1%)
Health	475 (33%)	391 (40%)
Experiencing Health problems or symptoms not due to Intervention	159 (11%)	158 (16%)
Worried about health effects of medical tests	6 (<1%)	3 (<1%)
Worried about costs if adverse effects occur	0 (0%)	4 (<1%)
Advised not to participate by health care provider	227 (16%)	167 (17%)
Study conflicts with health care needs	165 (11%)	144 (15%)
Expected more care	6 (<1%)	4 (<1%)
Intervention	583 (41%)	292 (30%)
Reports health problems or symptoms from WHI intervention	563 (39%)	254 (26%)
Problem with Clinic Practitioner or other CC staff	8 (1%)	2 (<1%)
Doesn't like taking pills	31 (2%)	28 (3%)
Doesn't like DM requirements	2 (<1%)	1 (<1%)
Problems with DM group Nutritionist or Group members	1 (<1%)	1 (<1%)
Doesn't like DM eating patterns	1 (<1%)	1 (<1%)
Doesn't like randomized nature of intervention	42 (3%)	22 (2%)
Expected some benefit from intervention	19 (1%)	16 (2%)
Won't participate in safety procedures	8 (1%)	4 (<1%)
Other	395 (27%)	267 (28%)
Not Given	152 (11%)	105 (11%)

[1] Multiple reasons may be reported for a woman

Table 4.9
Reports of Bleeding
Data as of: 8/31/97

	with Uterus
6 Week HRT Phone Call	
Number with an HRT Safety Interview	11414
Number with Bleeding	2684 (24%)
Semi-Annual Visit 1	
Number Having Visit	9371
Number with Bleeding	2729 (29%)
Annual Visit 1	
Number Having Visit	6483
Number with Bleeding	1218 (19%)
Semi-Annual Contact 2	
Number Having Visit	4317
Number with Bleeding	582 (13%)
Annual Visit 2	
Number Having Visit	2675
Number with Bleeding	302 (11%)
Semi-Annual Contact 3	
Number Having Visit	1544
Number with Bleeding	142 (9%)
Annual Visit 3	
Number Having Visit	692
Number with Bleeding	57 (8%)
Semi-Annual Contact 4	
Number Having Visit	77
Number with Bleeding	5 (6%)
Non Routine Contact	
Number Having Visit	12922
Number with Bleeding	1020 (8%)

Table 4.10
Other HRT Symptoms
Data as of: 8/31/97

	without Uterus	with Uterus
6 Week HRT Phone Call		
Number with an HRT Safety Interview	7342	11414
Number with Breast Changes	481 (7%)	848 (7%)
Semi-Annual Visit 1		
Number with an HRT Safety Interview	5918	9147
Number with Breast Changes	304 (5%)	554 (6%)
Annual Visit 1		
Number with an HRT Safety Interview	4176	6331
Number with Breast Changes	155 (4%)	258 (4%)
Semi-Annual Contact 2		
Number with an HRT Safety Interview	2609	4001
Number with Breast Changes	69 (3%)	127 (3%)
Annual Visit 2		
Number with an HRT Safety Interview	1723	2535
Number with Breast Changes	59 (3%)	87 (3%)
Semi-Annual Contact 3		
Number with an HRT Safety Interview	965	1373
Number with Breast Changes	26 (3%)	34 (2%)
Annual Visit 3		
Number with an HRT Safety Interview	468	653
Number with Breast Changes	11 (2%)	23 (4%)
Semi-Annual Contact 4		
Number with an HRT Safety Interview	45	71
Number with Breast Changes	1 (2%)	1 (1%)
Non Routine Contact		
Number Randomized	8408	12925
Number with Breast Changes	40 (<1%)	153 (1%)

Table 4.11
Endometrial Aspiration Results

Days since randomized	N of aspirations[1,2]	Number with Abnormal Results[3]				
		Cystic	Adenomatous	Atypia	Cancer	Total
0-90	127	1	0	1	0	1
91-180	152	2	0	1	0	1
181-270	145	3	2	0	0	2
271-360	108	4	2	1	0	3
361-450	90	1	0	0	0	0
451-540	75	1	0	1	0	1
541-630	53	2	0	1	1	2
631-720	44	2	0	0	0	0
721-810	37	3	0	0	1	1
811-900	34	3	1	0	0	1
901-990	21	2	0	0	0	0
991-1080	13	0	0	0	0	0
1081-1170	4	0	0	0	0	0
1171-1260	0	0	0	0	0	0
1261-1350	0	0	0	0	0	0
1351-1410	0	0	0	0	0	0
Total	913	24	5	5	2	12

[1] All endometrial aspirations after first adenomatous or worse result removed. If participants had more than one endometrial aspiration within a 30 day period, the latest was used.

[2] ERT-TO-PERT removed

[3] Abnormal results are based on local readings with the following groupings defined as follows:

Cystic is cystic hyperplasia without atypia

Adenomatous is adenomatous hyperplasia without atypia

Atypia is atypia or cystic or adenomatous hyperplasia with atypia

Row totals combine ademonatous, atypias and cancer catcgories

5. DM Intervention Status

5.1 Adherence

Nutrient intake data for adherence monitoring are presented in *Tables 5.1a-d.* Studywide, the mean difference between Intervention and Comparison women at AV-1 is 11.2% energy from fat, at AV-2 is 9.8%, and at AV-3 is 8.9%. While these Comparison - Intervention (C-I) differences represent a substantial achievement, they fall short of the original assumptions of 16% C-I at AV-1 subsequent decline of 1.4% per year. Approximately 3% of the 5% difference at AV-1 between the design and realized differences can be attributed to lower than anticipated % energy from fat at baseline, while the remaining difference relates to less than full achievement of intervention goals. A 13% C-I difference at AV-1, declining to an 11% difference by 9 years from randomization, preserves the protocol-defined study power in the DM, while acknowledging the lower than anticipated % energy from fat at baseline.

The reduced fat gram goals introduced Fall 1995 may be able to yield about a 0.8% increase (10.7% to 11.6%) in the C-I value by the end of recruitment. By the end of recruitment, approximately 80% of DM Intervention participants will have the reduced fat gram goals. Presently, 77% of DM Intervention participants have reduced Fat gram goals, though only about 61% of DM Intervention participants with an AV1 FFQ have the reduced fat gram goals (*Table 5.1b*). The C-I value in Minority women is considerably smaller (9.1%) at AV-1 than the overall results (*Table 5.1c*). Women over age 70 are also somewhat less adherent (*Table 5.1d*).

Multivariate analyses were conducted to examine where further increases in the C-I difference may arise (*Table 5.2a,b,c,d,e*). Age, race/ethnicity, and BMI are significant subject characteristic predictors of the C-I difference in fat intake in this regression analysis (*Table 5.2a*). Several DM participation variables including group size, session attendance and the value of the fat gram goal have significant impact on the C-I difference (*Table 5.2b*). The effects of psychosocial dietary and physical activity factors are presented in *Table 5.2c,d*, and *e*, respectively. (For descriptions of the psychosocial behavioral constructs, see Appendix A.) Positive responses to psychosocial questions are associated with better DM adherence. Having personal health-related conditions, such as diabetes or diverticulitis, impacts negatively on C-I percent energy from fat. Having personal dietary regimens (any special diet including diabetic or low calorie) impacts negatively on C-I percent energy from fat. Higher physical activity responses are associated with lower C-I energy from fat. For both health-related conditions and physical activity, one potential reason for the negative impact on adherence is that percent energy from fat might be lower upon entry to the WHI. The C-I mean difference in body weight change from Baseline to AV-1 is correlated positively with C-I percent energy from fat at AV-1. Further data analysis on body weight change and DM adherence is warranted, particularly regarding the potential of using short-term body weight change as a biomarker or predictor of DM adherence within the first year of Intervention. Study performance on these process factors are presented in *Table 5.3 - Intervention Group Formation* and *Table 5.4 (a-c) - Intervention Program Adherence Summary.*

Further specialized efforts directed to participant groups with lower C-I differences, e.g., minority populations and older women, and to Clinical Centers having smaller C-I difference have been underway through the PMC conference calls and adherence visits with Clinical Centers.

Body weight data (C-I) are presented in *Table 5.5a-c*. Body weight loss can be viewed as an indirect measure of adherence as it is difficult in a free-living setting to maintain the same energy intake while consuming a low-fat dietary pattern instead of a higher fat dietary pattern. However, weight loss is not a goal of the DM Intervention, thus an expected amount of weight loss is difficult to quantify. The Intervention group lost slightly more weight than the control group at AV1, though this difference does appear to be maintained at AV2.

One feature of the DM Intervention program to help adherence is Additional Assistance. The Additional Assistance procedure calls for nutritionists to meet with participants who are exceeding their fat gram goals or are not self-monitoring. Additional Assistance is being conducted sporadically among Clinical Centers due in part to high staff demands as recruitment, Intervention, and maintenance activities are in progress simultaneously. The CCC has developed reports to track Additional Assistance contacts and will be surveying Clinical Centers with the goal of promoting Additional Assistance contacts. Further, the CCC and three VCCs are developing a program to study motivational interviewing as a core interview process for the Additional Assistance contacts.

The CCC is undertaking three specific efforts to address maintenance of dietary change. First, the CCC is convening an expert group of behavior and dietary changes scientists to discuss long-term maintenance strategies for the WHI. This consultant group is composed of behavioral scientists external and internal to WHI. The group will meet twice by conference call and once for an all-day meeting to discuss existing maintenance strategies for the WHI and to recommend additional strategies if warranted. Second, the CCC in collaboration with three Clinical Centers is developing a program to study ways to enhance the peer support process. Third, the CCC is surveying Clinical Centers regarding implementation of the existing peer group meeting procedures. Currently, peer groups are encouraged, but not required, to meet between quarterly maintenance sessions led by nutritionists. Peer group attendance varies among Clinical Centers. The CCC is assessing how Clinical Centers implement the peer group process and soliciting ideas to improve their effectiveness from Clinical Centers who routinely conduct peer group sessions.

5.2 Adherence to Follow-up

Table 5.6 summarizes adherence to follow-up contacts by treatment arm and contact type. Retention of participants has been equivalent in the two arms, indicating that the reporting of event rates between arms should not be biased by poorer follow-up rates in the controls. The overall rates are well above the acceptable rates specified by the Steering Committee for collection of outcome data (90% at AV-1, decline of no more that 1% per year) but somewhat lower than program goals (98% at AV1, decline of no more than 1/2% per year).

Two percent (n=325) of women randomized to DM Intervention have stopped Intervention. Reasons for stopping DM Intervention are listed in *Table 5.7*. The main reasons given by participants include personal, not liking the DM Intervention or eating pattern, and health problem(s) not related to the Intervention. Women re contacted periodically (e.g., every 6 months)

by Clinic staff to talk about the reasons why the women stopped the intervention and if they are able or willing to consider re-starting the DM Intervention. Women who have stopped the Intervention continue to participate in follow-up clinic visits, unless they request not to be followed up. One percent of participants in DM Intervention and one percent in DM Control have requested not to be followed-up.

5.3 Safety

We define WHI DM safety as not compromising the nutritional status of participants due to participating in the WHI DM. We assess nutritional status using estimated nutrient intake and weight loss, comparing the Intervention group to the Control (Comparison) group. Dietary fat is the sole reductive goal of the WHI DM Intervention (Dietary Change). Thus, for the safety of women randomized to the WHI DM Intervention we monitor fat intake primarily, and weight loss secondarily as a marker of decreased fat intake.

By examining the lower tail of the fat intake distribution, e.g., 5th and 10th percentiles, we can estimate adequacy of fat intake (*Tables 5.8a* and *5.8b*). We can measure the adequacy of fat intake in the WHI DM Intervention relative to the FAO/WHO guidelines for fat intake for adults. The FAO/WHO guidelines suggest that most adults should consume at least 15% energy from fat in order to meet essential fatty acid and fat-soluble vitamin requirements. WHI Food Frequency data show that the 5th percentile for percentage energy from fat is 14.2% for Intervention participants and 24.2% for Control participants one year post-randomization. In fact, the actual 5th percentile will be higher than 14.2% for DM Intervention participants upon acknowledging the major random (and systematic) measurement error in the FFQ self-report of percent energy from fat.

Body weight loss data for participants who have lost more than 10 pounds between Baseline and AV-1 are shown in *Table 5.9b*. We selected a 10 pound weight loss to monitor as this is the weight loss that the Nutrition Screening Initiative for Older Americans recommends monitoring. We expect some weight loss and view this as an indicator of adherence to the Intervention. Excessive and undesirable weight loss in the DM Intervention participants warrants follow-up as an indicator of possibly compromised nutritional safety. We will continue to refine study monitoring of safety including efficient ways to identify DM Intervention participants who have experienced undesirable weight loss of 10 or more pounds and intervene appropriately.

Procedures exist for WHI nutritionists to assess the overall nutritional balance of DM Intervention participants. Nutritionists and DM Intervention participants meet once individually during the first year of Intervention to discuss adherence and safety (WHI Manuals: Volume 2 *Procedures*, Section 6 *Dietary Modification*). During this individual session, the nutritionists and participants review self-monitored food intake records and identify areas to change. Nutritionists meet with participants individually as needed to discuss any concerns expressed by participants regarding the DM Intervention, ranging from nutrient intake to quality of life issues. To date, most participant-generated requests for individual visits with a nutritionist have included concerns about consuming too little fat, hair loss, dry nails, dry skin, and compatibility of the low-fat dietary pattern with other special needs (e.g., weight loss, diabetes).

Table 5.1a
Nutrient Intake Monitoring

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
% Energy from Fat									
FFQ Baseline	15891	38.8	5.0	23831	38.9	5.0	0.1	0.1	0.18
FFQ Year 1[3]	8795	24.4	7.3	12869	35.6	6.9	11.2	0.1	0.00
FFQ Year 2[4]	1276	25.3	7.2	1945	35.1	7.0	9.8	0.3	0.00
FFQ Year 3[5]	143	25.5	7.8	194	34.4	6.5	8.9	0.8	0.00
4DFR Baseline	648	33.2	6.4	987	33.1	6.7	0.2	0.3	0.65
4DFR Year 1	348	22.0	7.4	563	32.7	6.4	10.7	0.5	0.00
24 Hr Recall, post-Baseline	130	22.8	9.6	180	31.9	7.3	9.1	1.0	0.00
24 Hr Recall, Year 1	58	22.6	7.7	84	31.8	7.9	9.2	1.3	0.00
24 Hr Recall, Year 2	18	26.5	12.3	24	34.2	7.5	7.7	3.1	0.00
Total Energy (kcal)									
FFQ Baseline	15891	1792	715	23831	1795	709	3	7	0.66
FFQ Year 1	8795	1491	534	12869	1587	641	96	8	0.00
FFQ Year 2	1276	1515	520	1945	1570	610	55	21	0.13
FFQ Year 3	143	1535	572	194	1558	644	23	68	0.94
4DFR Baseline	648	1715	459	987	1726	456	12	23	0.55
4DFR Year 1	348	1457	348	563	1631	430	173	27	0.00
24 Hr Recall, post-Baseline	130	1514	407	180	1661	509	148	54	0.01
24 Hr Recall, Year 1	58	1522	415	84	1634	444	112	74	0.14
24 Hr Recall, Year 2	18	1448	342	24	1733	584	285	155	0.09
Total Fat (g)									
FFQ Baseline	15891	78.0	35.4	23831	78.1	34.9	0.2	0.4	0.43
FFQ Year 1	8795	40.7	21.2	12869	63.8	31.5	23.1	0.4	0.00
FFQ Year 2	1276	42.6	19.8	1945	62.4	30.1	19.8	1.0	0.00
FFQ Year 3	143	44.5	25.6	194	60.7	30.6	16.2	3.2	0.00
4DFR Baseline	648	64.0	23.9	987	64.4	24.3	0.3	1.2	0.96
4DFR Year 1	348	35.5	14.8	563	60.0	22.0	24.5	1.3	0.00
24 Hr Recall, post-Baseline	130	39.2	22.0	180	60.4	26.4	21.2	2.8	0.00
24 Hr Recall, Year 1	58	39.2	19.8	84	58.8	23.7	19.6	3.8	0.00
24 Hr Recall, Year 2	18	42.3	20.3	24	67.7	31.0	25.4	8.4	0.00

[1] Absolute difference

[2] P-values bases on testing in the natural log scale except for % Energy from fat

[3] 2702 (31%) Intervention women had ≤ 20% energy from fat at year 1

[4] 310 (24%) Intervention women had ≤ 20% energy from fat at year 2

[5] 34 (24%) Intervention women had ≤ 20% energy from fat at year 3

Table 5.1a (continued)
Nutrient Intake Monitoring

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
Saturated Fat (g)									
FFQ Baseline	15891	27.5	13.5	23831	27.5	13.3	0.0	0.1	0.72
FFQ Year 1	8795	14.0	7.9	12869	22.4	11.9	8.4	0.1	0.00
FFQ Year 2	1276	14.6	7.3	1945	21.9	11.2	7.2	0.4	0.00
FFQ Year 3	143	15.2	9.8	194	21.6	12.1	6.5	1.2	0.00
4DFR Baseline	648	21.1	9.0	987	21.2	9.1	0.1	0.5	0.99
4DFR Year 1	348	11.1	5.3	563	19.5	7.9	8.4	0.5	0.00
24 Hr Recall, post-Baseline	130	12.8	7.9	180	20.2	9.8	7.4	1.0	0.00
24 Hr Recall, Year 1	58	12.7	7.2	84	19.3	9.4	6.6	1.5	0.00
24 Hr Recall, Year 2	18	13.5	7.5	24	21.7	10.1	8.2	2.8	0.01
Polyunsaturated Fat (g)									
FFQ Baseline	15891	15.5	7.7	23831	15.5	7.6	0.0	0.1	0.35
FFQ Year 1	8795	7.7	4.2	12869	12.4	6.7	4.7	0.1	0.00
FFQ Year 2	1276	7.9	4.1	1945	11.9	6.3	4.0	0.2	0.00
FFQ Year 3	143	8.5	5.1	194	11.3	5.9	2.8	0.6	0.00
4DFR Baseline	648	13.3	5.9	987	13.6	6.2	0.3	0.3	0.49
4DFR Year 1	348	7.6	3.4	563	12.6	5.7	5.0	0.3	0.00
24 Hr Recall, post-Baseline	130	8.2	5.1	180	12.3	7.0	4.1	0.7	0.00
24 Hr Recall, Year 1	58	8.0	4.7	84	12.3	6.7	4.2	1.0	0.00
24 Hr Recall, Year 2	18	7.9	3.8	24	14.4	7.9	6.5	2.0	0.00
Fruits and Vegetables (servings)									
FFQ Baseline	15797	3.6	1.8	23728	3.6	1.8	0.0	0.0	0.99
FFQ Year 1	8758	5.1	2.3	12833	3.8	2.0	1.3	0.0	0.00
FFQ Year 2	1274	5.2	2.4	1942	3.9	2.0	1.3	0.1	0.00
FFQ Year 3	143	5.3	2.3	194	4.0	2.0	1.3	0.2	0.00

[1] Absolute difference

[2] P-values bases on testing in the natural log scale except for % Energy from fat

Table 5.1b
Nutrient Intake Monitoring For Women With Revised Fat Gram Goals

	Intervention[1]			Control[2]			Difference		
	N	Mean	SD	N	Mean	SD	Mean[3]	SE	p-value[4]
% Energy from Fat									
FFQ Baseline	12176	38.8	5.0	18290	38.8	5.0	0.0	0.1	0.60
FFQ Year 1	5368	24.4	7.4	7898	35.8	6.8	11.5	0.1	0.00
FFQ Year 2	227	24.2	7.1	326	35.9	7.0	11.8	0.6	0.00
FFQ Year 3	9	22.6	5.9	8	35.4	4.5	12.8	2.6	0.00
4DFR Baseline	453	32.9	6.4	674	33.2	6.8	0.3	0.4	0.49
4DFR Year 1	156	22.5	8.1	250	33.1	6.4	10.7	0.7	0.00
Total Energy (kcal)									
FFQ Baseline	12176	1780	701	18290	1792	709	12	8	0.21
FFQ Year 1	5368	1486	532	7898	1598	648	112	11	0.00
FFQ Year 2	227	1494	469	326	1569	587	75	47	0.29
FFQ Year 3	9	1572	546	8	1550	433	21	241	0.92
4DFR Baseline	453	1693	468	674	1732	468	39	28	0.14
4DFR Year 1	156	1430	364	250	1618	414	188	40	0.00
Total Fat (g)									
FFQ Baseline	12176	77.3	34.5	18290	77.9	34.7	0.5	0.4	0.19
FFQ Year 1	5368	40.5	21.2	7898	64.6	32.0	24.1	0.5	0.00
FFQ Year 2	227	40.1	18.2	326	63.7	29.4	23.6	2.2	0.00
FFQ Year 3	9	38.6	16.0	8	59.5	12.8	20.9	7.1	0.05
4DFR Baseline	453	62.6	24.1	674	64.7	24.8	2.0	1.5	0.20
4DFR Year 1	156	35.7	16.6	250	60.2	21.9	24.5	2.0	0.00
Saturated Fat (g)									
FFQ Baseline	12176	27.2	13.2	18290	27.4	13.3	0.2	0.2	0.32
FFQ Year 1	5368	13.8	8.0	7898	22.6	12.1	8.7	0.2	0.00
FFQ Year 2	227	13.6	6.6	326	22.0	10.8	8.4	0.8	0.00
FFQ Year 3	9	12.6	6.3	8	20.9	4.8	8.3	2.7	0.01
4DFR Baseline	453	20.6	9.1	674	21.2	9.4	0.7	0.6	0.28
4DFR Year 1	156	11.2	5.8	250	19.0	7.6	7.8	0.7	0.00
Polyunsaturated Fat (g)									
FFQ Baseline	12176	15.2	7.5	18290	15.3	7.5	0.1	0.1	0.15
FFQ Year 1	5368	7.5	4.1	7898	12.4	6.7	4.9	0.1	0.00
FFQ Year 2	227	7.5	3.8	326	12.4	6.3	4.8	0.5	0.00
FFQ Year 3	9	7.2	2.7	8	11.2	3.2	4.0	1.4	0.01
4DFR Baseline	453	13.1	6.0	674	13.7	6.5	0.7	0.4	0.09
4DFR Year 1	156	7.6	3.6	250	13.1	6.3	5.5	0.6	0.00
Fruits and Vegetables (servings)									
FFQ Baseline	12120	3.6	1.8	18232	3.6	1.8	0.0	0.0	0.94
FFQ Year 1	5363	5.1	2.3	7888	3.9	2.0	1.3	0.0	0.00
FFQ Year 2	227	5.4	2.2	326	4.1	2.0	1.3	0.2	0.00
FFQ Year 3	9	6.1	3.1	8	4.1	1.3	2.0	1.2	0.18

[1] Intervention group is defined as women randomized to Intervention after 6/15/95 that have revised fat gram goals.
[2] Control group is defined as women randomized to Control after 6/15/95.
[3] Absolute difference
[4] P-values bases on testing in the natural log scale except for % Energy from fat

Table 5.1c
Nutrient Intake Monitoring in Minority Women

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
% Energy from Fat									
FFQ Baseline	2896	39.3	5.1	4258	39.5	5.2	0.2	0.1	0.12
FFQ Year 1[3]	1382	26.9	8.1	1958	36.0	7.4	9.1	0.3	0.00
FFQ Year 2[4]	167	27.2	7.8	230	35.2	7.2	8.0	0.8	0.00
FFQ Year 3[5]	10	29.2	8.8	19	34.3	6.8	5.0	3.0	0.12
4DFR Baseline	304	33.6	6.3	449	33.7	6.8	0.1	0.5	0.87
4DFR Year 1	114	23.5	7.8	180	33.4	6.7	10.0	0.9	0.00
24 Hr Recall, post-Baseline	21	26.7	11.5	29	31.7	7.9	5.0	2.7	0.03
24 Hr Recall, Year 1	7	23.1	8.1	8	29.5	7.3	6.4	4.0	0.13
24 Hr Recall, Year 2	4	31.2	19.3	2	39.0	6.8	7.8	14.8	0.35
Total Energy (kcal)									
FFQ Baseline	2896	1760	812	4258	1762	828	2	20	0.81
FFQ Year 1	1382	1421	607	1958	1490	782	69	25	0.14
FFQ Year 2	167	1427	613	230	1567	763	140	72	0.14
FFQ Year 3	10	1770	926	19	1449	700	321	306	0.41
4DFR Baseline	304	1671	477	449	1697	471	25	35	0.38
4DFR Year 1	114	1369	362	180	1565	438	196	49	0.00
24 Hr Recall, post-Baseline	21	1301	443	29	1655	421	355	123	0.02
24 Hr Recall, Year 1	7	1668	539	8	1499	287	169	219	0.49
24 Hr Recall, Year 2	4	1331	324	2	1865	110	534	248	0.06
Total Fat (g)									
FFQ Baseline	2896	77.7	39.8	4258	78.1	40.5	0.4	1.0	0.86
FFQ Year 1	1382	42.8	24.8	1958	60.8	37.0	18.0	1.1	0.00
FFQ Year 2	167	42.8	21.8	230	62.5	36.2	19.7	3.1	0.00
FFQ Year 3	10	62.3	47.1	19	55.5	28.5	6.8	14.0	1.00
4DFR Baseline	304	62.9	23.0	449	64.6	25.6	1.7	1.8	0.56
4DFR Year 1	114	36.0	16.9	180	59.1	22.8	23.1	2.5	0.00
24 Hr Recall, post-Baseline	21	37.1	16.9	29	59.2	23.7	22.1	6.1	0.00
24 Hr Recall, Year 1	7	43.9	22.8	8	50.0	18.6	6.1	10.7	0.56
24 Hr Recall, Year 2	4	47.1	31.7	2	80.8	19.4	33.6	25.2	0.16

[1] Absolute difference

[2] P-values bases on testing in the natural log scale except for % Energy from fat

[3] 286 (21%) Minority Intervention women had ≤ 20% energy from fat at year 1

[4] 30 (18%) Minority Intervention women had ≤ 20% energy from fat at year 2

[5] 2 (20%) Minority Intervention women had ≤ 20% energy from fat at year 3

Table 5.1c (continued)
Nutrient Intake Monitoring in Minority Women

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
Saturated Fat (g)									
FFQ Baseline	2896	26.0	14.2	4258	26.2	14.7	0.2	0.3	0.86
FFQ Year 1	1382	14.2	8.8	1958	20.2	13.3	6.1	0.4	0.00
FFQ Year 2	167	14.1	7.5	230	21.1	12.9	7.0	1.1	0.00
FFQ Year 3	10	19.0	15.0	19	19.7	13.0	0.7	5.4	0.49
4DFR Baseline	304	20.0	8.4	449	20.6	9.3	0.6	0.7	0.51
4DFR Year 1	114	11.1	5.8	180	18.4	7.7	7.4	0.8	0.00
24 Hr Recall, post-Baseline	21	11.1	5.4	29	19.6	9.4	8.5	2.3	0.00
24 Hr Recall, Year 1	7	14.7	9.6	8	13.0	4.6	1.7	3.8	1.00
24 Hr Recall, Year 2	4	15.4	11.4	2	22.7	4.2	7.3	8.8	0.35
Polyunsaturated Fat (g)									
FFQ Baseline	2896	15.9	8.7	4258	15.9	8.6	0.0	0.2	0.81
FFQ Year 1	1382	8.4	5.0	1958	12.4	7.7	3.9	0.2	0.00
FFQ Year 2	167	8.4	4.7	230	12.3	7.4	4.0	0.7	0.00
FFQ Year 3	10	13.5	10.7	19	10.4	4.4	3.1	2.8	0.89
4DFR Baseline	304	13.6	6.2	449	14.0	6.8	0.3	0.5	0.55
4DFR Year 1	114	7.8	3.7	180	12.9	6.3	5.1	0.6	0.00
24 Hr Recall, post-Baseline	21	8.4	4.1	29	11.9	6.5	3.6	1.6	0.04
24 Hr Recall, Year 1	7	8.9	4.6	8	13.4	6.0	4.5	2.8	0.16
24 Hr Recall, Year 2	4	7.8	3.3	2	17.2	5.7	9.4	3.5	0.06
Fruits and Vegetables (servings)									
FFQ Baseline	2881	3.2	1.9	4251	3.2	1.9	0.1	0.0	0.11
FFQ Year 1	1376	4.6	2.5	1955	3.4	2.0	1.3	0.1	0.00
FFQ Year 2	166	4.8	2.7	229	3.6	2.0	1.2	0.2	0.00
FFQ Year 3	10	5.5	2.7	19	3.9	2.3	1.7	1.0	0.08

[1] Absolute difference

[2] P-values bases on testing in the natural log scale except for % Energy from fat

Table 5.1d
Nutrient Intake Monitoring in Women Aged 70-79

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
% Energy from Fat									
FFQ Baseline	2463	38.4	4.7	3702	38.4	4.8	0.0	0.1	0.83
FFQ Year 1[3]	1207	25.5	7.2	1786	35.6	6.3	10.1	0.2	0.00
FFQ Year 2[4]	173	26.8	7.9	270	34.8	6.7	8.0	0.7	0.00
FFQ Year 3[5]	21	29.2	9.8	24	38.2	6.8	9.0	2.5	0.00
4DFR Baseline	89	31.7	5.5	130	33.2	6.5	1.4	0.8	0.09
4DFR Year 1	44	22.8	6.1	71	34.0	5.9	11.3	1.1	0.00
24 Hr Recall, post-Baseline	21	22.9	9.0	24	32.0	6.9	9.1	2.4	0.00
24 Hr Recall, Year 1	9	23.5	8.6	11	30.8	6.2	7.3	3.3	0.05
Total Energy (kcal)									
FFQ Baseline	2463	1675	645	3702	1690	665	15	17	0.55
FFQ Year 1	1207	1437	546	1786	1535	622	98	22	0.00
FFQ Year 2	173	1450	488	270	1456	578	6	53	0.75
FFQ Year 3	21	1584	816	24	1309	538	275	204	0.39
4DFR Baseline	89	1576	391	130	1655	430	78	57	0.17
4DFR Year 1	44	1382	301	71	1507	389	125	69	0.11
24 Hr Recall, post-Baseline	21	1500	405	24	1663	401	164	120	0.20
24 Hr Recall, Year 1	9	1443	452	11	1418	361	26	182	0.24
Total Fat (g)									
FFQ Baseline	2463	72.1	31.2	3702	72.6	32.1	0.6	0.8	0.64
FFQ Year 1	1207	41.3	22.9	1786	61.6	29.7	20.3	1.0	0.00
FFQ Year 2	173	43.1	20.5	270	57.1	27.5	14.0	2.4	0.00
FFQ Year 3	21	55.2	40.1	24	55.1	23.6	0.1	9.7	0.45
4DFR Baseline	89	56.5	20.6	130	62.0	23.2	5.5	3.1	0.09
4DFR Year 1	44	34.8	11.6	71	57.6	19.3	22.8	3.2	0.00
24 Hr Recall, post-Baseline	21	39.3	22.1	24	59.9	21.0	20.5	6.4	0.00
24 Hr Recall, Year 1	9	38.7	21.7	11	49.0	17.9	10.2	8.9	0.16

[1] Absolute difference

[2] P-values bases on testing in the natural log scale except for % Energy from fat

[3] 291 (24%) Intervention women aged 70-79 had ≤ 20% energy from fat at year 1

[4] 31 (18%) Intervention women aged 70-79 had ≤ 20% energy from fat at year 2

[5] 3 (14%) Intervention women aged 70-79 had ≤ 20% energy from fat at year 3

Table 5.1d (continued)
Nutrient Intake Monitoring in Women Aged 70-79

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
Saturated Fat (g)									
FFQ Baseline	2463	25.4	12.0	3702	25.5	12.4	0.1	0.3	0.90
FFQ Year 1	1207	14.4	8.5	1786	21.6	11.3	7.2	0.4	0.00
FFQ Year 2	173	14.9	7.5	270	20.1	10.8	5.2	0.9	0.00
FFQ Year 3	21	19.8	17.8	24	19.8	9.4	0.0	4.2	0.26
4DFR Baseline	89	19.2	7.7	130	20.7	8.8	1.5	1.1	0.27
4DFR Year 1	44	11.2	4.6	71	19.2	7.0	8.0	1.2	0.00
24 Hr Recall, post-Baseline	21	11.6	6.5	24	21.9	9.8	10.3	2.5	0.00
24 Hr Recall, Year 1	9	14.4	10.1	11	16.3	6.4	2.0	3.7	0.38
Polyunsaturated Fat (g)									
FFQ Baseline	2463	14.4	7.0	3702	14.5	7.1	0.1	0.2	0.62
FFQ Year 1	1207	7.8	4.7	1786	12.0	6.2	4.3	0.2	0.00
FFQ Year 2	173	8.1	5.0	270	10.9	5.5	2.9	0.5	0.00
FFQ Year 3	21	10.0	6.3	24	9.9	5.5	0.1	1.8	0.78
4DFR Baseline	89	11.2	4.6	130	12.9	6.2	1.7	0.8	0.04
4DFR Year 1	44	7.0	2.4	71	12.1	4.8	5.1	0.8	0.00
24 Hr Recall, post-Baseline	21	8.8	5.6	24	10.7	5.3	1.8	1.6	0.12
24 Hr Recall, Year 1	9	7.4	4.4	11	9.3	3.6	1.9	1.8	0.16
Fruits and Vegetables (servings)									
FFQ Baseline	2453	3.8	1.8	3690	3.9	1.9	0.1	0.0	0.24
FFQ Year 1	1203	5.1	2.2	1783	4.1	2.0	1.0	0.1	0.00
FFQ Year 2	173	5.2	2.6	269	3.9	1.8	1.3	0.2	0.00
FFQ Year 3	21	5.2	1.8	24	3.3	1.7	1.9	0.5	0.00

[1] Absolute difference

[2] P-values bases on testing in the natural log scale except for % Energy from fat

Table 5.2a
Control - Intervention Difference in % Energy from Fat from FFQ at AV1:
Multivariate Analysis of Study Subject Characteristics
Data as of: 8/31/97

Study Subject Characteristics		C - I (%)
Age	50-54 vs. 60-69	0.71**
	55-59 vs. 60-69	0.27
	70-79 vs. 60-69	-1.07**
Ethnicity	Black vs. White	-2.25**
	Hispanic vs. White	-1.84**
	Other Minority vs. White	-0.91
Education	0-8 Years vs. Post H.S.	1.05
	Some H.S. or Diploma vs. Post H.S.	0.11
Family Income	<20K vs. ≥75K	-0.35
	20-35K vs. ≥75K	-0.40
	35-50K vs. ≥75K	0.17
	50-75K vs. ≥75K	-0.59
HRT Randomized	Yes vs. No	0.18
BMI - Mean(BMI)	BMI - 29.03	-0.02**
Hysterectomy	Yes vs. No	0.23

* Indicates p-value < .05 from two-sided t-test
** Indicates p-value < .01 from two-sided t-test
NOTE: Model adjusted for clinic effects

Table 5.2a (continued)
Control - Intervention Difference in % Energy from Fat from FFQ at AV2:
Multivariate Analysis of Study Subject Characteristics
Data as of: 8/31/97

Study Subject Characteristics		C - I (%)
Age	50-54 vs. 60-69	-0.70
	55-59 vs. 60-69	0.02
	70-79 vs. 60-69	-2.24**
Ethnicity	Black vs. White	-3.37**
	Hispanic vs. White	0.42
	Other Minority vs. White	1.79
Education	0-8 Years vs. Post H.S.	1.15
	Some H.S. or Diploma vs. Post H.S.	0.57
Family Income	<20K vs. >75K	-0.62
	20-35K vs. >75K	-0.21
	35-50K vs. >75K	0.08
	50-75K vs. >75K	0.17
HRT Randomized	Yes vs. No	-0.24
BMI - Mean(BMI)	BMI - 29.03	-0.10*
Hysterectomy	Yes vs. No	0.37

* Indicates p-value < .05 from two-sided t-test
** Indicates p-value < .01 from two-sided t-test
NOTE: Model adjusted for clinic effects

Table 5.2b
Effects of DM Intervention Participation Variables
on Control - Intervention % Energy from Fat at AV1
Data as of: 8/31/97

DM Implementation/Participation	C-I % Energy from Fat[1]	C-I % Energy from Fat[2]	C-I % Energy from Fat[3]
Intervention Group Size	0.08**	0.07**	0.08**
Days from Randomization to Intervention Group/100	-0.09	-0.14	-0.12
# Sessions (out of 1-18) Attended	0.42**		0.25**
# Sessions (out of 1-18) Completed	0.35**		0.04
Fat Gram Goal	-0.04*	-0.04*	-0.04*
# Early Sessions Completed (1-6)		0.50**	
# Intermediate Sessions Completed (7-12)		1.14**	
# Late Sessions Completed (13-18)		0.49**	
# Sessions (out of 3-18) Providing Fat Scores			0.49**

[1] Model adjusted for clinic effects, and includes the following terms: Intervention group size, days from randomization to group assignment, # sessions attended, # sessions completed, and fat gram goal.

[2] Model adjusted for clinic effects, and includes the following terms: Intervention group size, days from randomization to group assignment, fat gram goal, # early sessions completed, # intermediate sessions completed, and # late sessions completed.

[3] Model adjusted for clinic effects, and includes the following terms: Intervention group size, days from randomization to group assignment, # sessions attended, # sessions completed, fat gram goal, and #sessions fat score provided.

* Indicates p-value < .05 from two-sided t-test

** Indicates p-value < .01 from two-sided t-test

Table 5.2b (continued)
Effects of DM Intervention Participation Variables
on Control - Intervention % Energy from Fat at AV2
Data as of: 8/31/97

DM Implementation/Participation	C-I % Energy from Fat[1]	C-I % Energy from Fat[2]	C-I % Energy from Fat[3]
Intervention Group Size	-0.09	-0.08	-0.10
Days from Randomization to Intervention Group/100	0.0001	-0.0004	0.0009
# Sessions (out of 1-18) Attended	0.45**		0.36**
# Sessions (out of 1-18) Completed	0.50**		0.33*
Fat Gram Goal	-0.17**	-0.16**	-0.18**
# Early Sessions Completed (1-6)		-0.05	
# Intermediate Sessions Completed (7-12)		1.28**	
# Late Sessions Completed (13-18)		1.00**	
# Sessions (out of 3-18) Providing Fat Scores			0.26**

[1] Model adjusted for clinic effects, and includes the following terms: Intervention group size, days from randomization to group assignment, # sessions attended, # sessions completed, and fat gram goal.

[2] Model adjusted for clinic effects, and includes the following terms: Intervention group size, days from randomization to group assignment, fat gram goal, # early sessions completed, # intermediate sessions completed, and # late sessions completed.

[3] Model adjusted for clinic effects, and includes the following terms: Intervention group size, days from randomization to group assignment, # sessions attended, # sessions completed, fat gram goal, and #sessions fat score provided.

* Indicates p-value < .05 from two-sided t-test

** Indicates p-value < .01 from two-sided t-test

Table 5.2c
Psychosocial Predictors of Adherence to DM

Baseline (Form 37) and Year 1 (Form 38) psychosocial variables in relation to DM adherence in selected time periods. Adherence analyses are based on all women providing a food frequency estimate of % energy from fat at AV-1 or AV-2. The following demographic variables were included in the regression model: age, ethnicity, education, income, body mass index, hysterectomy status, and HRT randomized. Each entry is the estimated change in C-I% energy from fat associated with an upward shift of one standard deviation in the psychosocial variable. An asterisk denotes statistical significance at the 0.05 level (from regression t-test).

Psychosocial Behavioral Constructs[a]	Baseline to AV-1 Form 37	AV-1 to AV-2 Form 37	AV-1 to AV-2 Form 38
(Number of Women)	(21664)	(3221)	(3086)
Social Support Construct (Higher score indicates greater support)	0.17	0.36	
Social Strain Construct[b] (Higher score indicates less strain)	0.16	0.34	
Optimism Construct (Higher score indicates more optimism)	0.41*	0.79*	
Negative Emotional Expressiveness[b] (Higher score indicates less negative expressiveness)	0.22*	0.23	
Ambivalent Emotional Expressiveness[b] (Higher score indicates less ambivalence)	0.15	-0.06	
Hostility Construct[b] (Higher score indicates less hostility)	0.27*	0.63*	
Overall Quality of Life (Form 37, Qx. 46. Higher score indicates higher perceived quality)	0.31*	0.58*	0.80*
Satisfaction with Quality of Life (Form 37, Qx. 47. Higher score indicates more satisfaction)	0.36*	0.41	0.90*
Physical Function Const. (Higher score indicates less limitations)	0.29*	0.30	0.58*
Limitations Due to Physical Health Const.(Higher score indicates less limitations)	0.39*	0.28	0.65*
Limitations Due to Emotional Problems Const. (Higher score indicates less limitations)	0.37*	-0.10	0.30
Health Interference with Social Activities (Form 37, Qx. 74. Higher score indicates less interference)	0.31*	0.07	0.46
Downhearted and Blue (Form 37, Qx. 80. Higher score indicates less feeling blue)	0.35*	0.54*	0.62*
Feel Worn Out (Form 37, Qx. 81. Higher score indicates less worn out)	0.25*	0.63*	0.55*
Pain Construct (Higher score indicates less pain)	0.27*	0.60*	0.58*
General Health Const. (Higher score indicates better health)	0.51*	0.67*	0.98*
Daily Living Activities Construct[b] (Higher score indicates less disability)	-0.30*	0.46	0.45
Overall Symptom Construct[b] (Higher score indicates fewer symptoms)	0.66*	0.63	0.49
Life Event Construct[b] (Higher score indicates fewer and less upsetting life events)	0.27*	0.25	0.28
CES-D/DIS Depression Construct[b] (Higher score indicates less depression)	0.33*	0.44	0.29
Worried that sex will affect health[b] (Form 37, Qx. 124. Higher score indicates less worried)	0.39*	0.67*	0.35

a - For descriptions of the psychosocial behavioral constructs, see Appendix A.

b - The sign of the parameter was reversed to reflect the description of the scoring.

Table 5.2d
Regression Analysis of DM Participants:Control-Intervention Difference in % Energy from Fat (FFQ) at Annual Visit 1 (AV1) and Annual Visit 2 (AV2)
Dietary Variables
Data as of 8/31/97

The following demographic variables were included in the regression model: age, ethnicity, education, income, body mass index, hysterectomy status, and HRT randomized.

NOTE: An asterisk denotes statistical significance at the 5% level (from regression t-test).

NOTE: Underlining denotes reference level.

			DM (n=21664)		DM (n=3221)	
			DM Participants with a %Energy from Fat at AV1		DM Participants with a %Energy from Fat at AV2	
Form/ Question #	Question		% Yes	C-I	%Yes	C-I
2/3, 23	Did a doctor ever say that you had sugar diabetes or high blood sugar when you were not pregnant?	Yes vs. No	4.9	-1.38*	4.0	-0.48
30, 2	Has a doctor told you that you have any of the following conditions or have you had any of the following procedures? (Please mark all that apply.)					
2.3*	High cholesterol requiring pills	Yes vs. No	9.7	-1.67*	9.7	-2.18
2.8	Stomach or duodenal ulcer	Yes vs. No	6.6	0.02	7.1	-1.48
2.9*	Diverticulitis	Yes vs. No	7.4	-1.13*	8.0	-0.56
2.10	Ulcerative colitis or Crohn's disease	Yes vs. No	0.9	-0.32	1.2	-3.80
2.16	Part of intestines taken out	Yes vs. No	1.4	-0.79	1.4	-3.85
30, 5	Did a doctor ever say that you had gallbladder disease or gallstones:	Yes vs. No	15.6	-0.42	15.1	-0.45
30, 7	Did a doctor ever say that you had hypertension or high blood pressure? (Do not include high blood pressure that you had only when you were pregnant.)	Yes vs. No	31.6	0.002	30.3	0.18
30, 10*	Have you ever had a colonoscopy or sigmoidoscopy or flex sig (where a doctor inserts a tube in the rectum to check for bowel problems)?	Yes vs. No	47.3	-0.70*	48.0	-0.46
2/3, 23.3	Did a doctor ever tell you to keep a special diet for your diabetes?	Yes vs. No	3.8	-1.29*	3.1	-1.39

Table 5.2d (continued)

Form/ Question #	Question		DM (n=21664) DM Participants with a %Energy from Fat at AV1		DM (n=3221) DM Participants with a %Energy from Fat at AV2	
			% Yes	C-I	%Yes	C-I
34, 5	The next set of questions are about special diets or types of foods women may choose or may be told to eat by their doctors. Are you now on any of the following special diets?					
5.1	A low calorie diet?	Yes vs. No	6.4	-1.58*	7.3	-2.92*
5.2	A low-fat or low cholesterol diet?	Yes vs. No	24.6	-2.06*	26.8	-2.17*
5.3	A low salt (low sodium) diet?	Yes vs. No	17.1	-1.28*	18.4	-1.37*
5.4	A high-fiber diet?	Yes vs. No	11.4	-1.67*	12.5	-1.46
5.5	A diabetic or ADA diet?	Yes vs. No	3.1	-2.01*	2.6	-2.35
5.6	A lactose-free (no milk or diary foods) diet?	Yes vs. No	3.7	-1.93*	4.0	-1.52
5.7	Any other diet?	Yes vs. No	5.5	-0.78	5.6	-0.32
45	Current Supplements	Yes vs. No	62.5	-0.17*	60.5	0.23
34, 1.7	Have you ever smoked to keep from gaining weight or to lose weight?	Yes vs. No	8.6	-0.82*	8.7	0.25
34, 4	Women's weights change during their adult lives. Mark the one answer that best describes you during your adult life. Please don't incllude times when you were pregnant or sick. (Mark only one.)					
4.2	Steady gain in weight vs. Weight has stayed about the same (within 10 pounds)		39.9	0.05	40.3	0.35
4.3	Lost weight as an adult and kept it off vs. Weight has stayed about the same (within 10 pounds)		1.4	-1.91*	1.4	-0.51
4.4	Weight has gone up and down again by more than 10 pounds vs. Weight has stayed about the same (within 10 pounds)		36.8	-0.05	36.9	-0.96
	Weight change from Baseline to AV-1 (Kg)		1.09[1]	0.07*	1.04[1]	0.08

[1] Mean difference

Table 5.2e
Regression Analysis of DM Participants -Control-Intervention Difference in % Energy from Fat (FFQ) at Annual Visit 1 (AV1) and Annual Visit 2 (AV2)
Physical Activity Variables
Data as of 8/31/97

The following demographic variables were included in the regression model: age, ethnicity, education, income, body mass index, hysterectomy status, and HRT randomized. Each entry is the estimated change in C-I percent energy from fat. An asterisk denotes statistical significance at the 0.05 level (from regression t-test).

	DM (n = 21664)		DM (n = 3221)	
	DM Participants with a %Energy from Fat at AV1		DM Participants with a %Energy from Fat at AV2	
Construct	Mean of Risk Factor[1]	C-I	Mean of Risk Factor[1]	C-I
Expenditure of energy (kcal/week*kg) from walking.	3.6	-0.02	3.6	-0.03
Episodes per week of physical activity (walking, hard, moderate, and mild exercise).	4.0	-0.07*	4.0	-0.16
Minutes per week of physical activity (walking, hard, moderate, and mild exercise).	141.5	-0.001	141.9	-0.002
Episodes per week of moderate and strenuous physical activity (MET >=4.0).	2.3	-0.11*	2.3	-0.24
Minutes per week of moderate and strenuous physical activity (MET >=4.0).	79.7	-0.002*	81.3	-0.01
Episodes per week of strenuous physical activity (MET >=6.0).	0.5	-0.19*	0.5	-0.68*
Minutes per week of strenuous physical activity (MET >=6.0).	21.5	-0.002	21.5	-0.01
Total expenditure (kcal/week*kg) from physical activity.	10.4	-0.01	10.5	-0.04
Episodes per week of physical activity of >=20 minutes duration per session.	3.1	-0.08*	3.1	-0.16
Episodes per week of moderate and strenuous physical activity of >=20 minutes duration per session (MET>=4.0).	1.7	-0.12*	1.8	-0.27*

[1] Inactive women included in the mean.

Table 5.3a
Intervention Group Formation

	VCC		NCC		Total	
	N	%	N	%	N	%
Randomized to Intervention	8017	--	7874	--	15891	--
Awaiting Intervention	663	8%	1949	25%	2612	16%
Waiting >= 20 weeks	291	44%	597	31%	888	34%
Number of DM Intervention Participants who Have Reached AV1 w/o Having Started Intervention[1]	211	3%	216	6%	427	4%
Intervention Started	7354	92%	5925	75%	13279	84%
Waited >=20 weeks	977	13%	919	16%	1896	14%
Number of Groups Started	625	--	468	--	1093	--
Number of DM Intervention Participants who Have Stopped Intervention	226	2.8%	99	1.3%	325	2.0%

[1] Includes Participants who have stopped Intervention.

Table 5.4a
Intervention Program Adherence Summary

	Intervention Session			
	4	**8**	**12**	**16**
Participants Assigned	13245	12757	10882	9058
Attendance[1]	85%	78%	71%	67%
Completion[2]	97%	94%	91%	88%
Self-Monitoring				
Fat gram				
Score obtained	92%	87%	83%	78%
Average score[3]	28.6	25.4	24.8	25.0
Average goal	26.7	26.8	27.3	27.8
% ≤ Fat Gram goal[1]	51%	66%	71%	72%
Fruit/Vegetable servings				
Score obtained	n.a.	85%	83%	78%
Average score[3]	n.a.	5.5	5.6	5.6
Goal	n.a.	≥ 5	≥ 5	≥ 5
% ≥ Fruit/Vegetable goal[3]	n.a.	55%	60%	62%
Grain servings				
Score obtained	n.a.	85%	83%	78%
Average score[3]	n.a.	4.9	5.1	5.4
Goal	n.a.	≥ 6	≥ 6	≥ 6
% ≥ Grain goal[3]	n.a.	19%	24%	29%
Additional Assistance[4] (for Fat Score >125% goal or No Score)	n.a.	26%	25%	28%

[1] The major reason given for not attending sessions is "busy", followed by "sick" or "family", then "transportation."

[2] Of participants assigned through Session 18, 9.8% did not complete (missed) 3 or more consecutive sesion, 6.3% missed 5 or more consecutive session, 3.8% missed 8 or more consecutive sessions (including participants who have stopped Intervention or stopped follow-up.

[3] Of participants providing a score.

[4] 21% of required Additional Assistance contacts were conducted.

Table 5.4b
Intervention Program Adherence Summary

Participants with Revised (Lower) Fat Gram Goals[1]

	Intervention Session			
	4	**8**	**12**	**16**
Participants Assigned	9594	9121	7275	5496
Attendance	84%	77%	70%	67%
Completion	97%	93%	89%	85%
Self-Monitoring				
Fat gram				
Score obtained	92%	85%	81%	75%
Average score[2]	27.5	24.2	23.2	23.0
Average goal	24.6	24.6	24.6	24.6
% ≤ Fat Gram goal[2]	47%	61%	67%	68%
Fruit/Vegetable servings				
Score obtained	n.a.	83%	81%	75%
Average score[2]	n.a.	5.6	5.6	5.7
Goal	n.a.	≥ 5	≥ 5	≥ 5
% ≥ Fruit/Vegetable goal[2]	n.a.	57%	62%	63%
Grain servings				
Score obtained	n.a.	83%	81%	75%
Average score[2]	n.a.	5.0	5.2	5.4
Goal	n.a.	≥ 6	≥ 6	≥ 6
% ≥ Grain goal[2]	n.a.	21%	25%	29%

[1] Implemented in women starting DM Intervention after September 15, 1995.

[2] Of participants providing a score

Table 5.4c
Intervention Program Adherence Summary
Maintenance Sessions

	Maintenance Session - Year 2			
	Spring	Summer	Fall	Winter
Participants Assigned	5596	6642	3576	4418
Attendance	65%	61%	64%	63%
Completion	83%	78%	85%	85%
Self-Monitoring				
Fat gram				
Score obtained	70%	64%	72%	70%
Average score[1]	25.8	25.9	27.3	27.3
Average goal	29.6	29.6	32.1	30.8
% ≤ Fat Gram goal[1]	75%	75%	80%	73%
Fruit/Vegetable servings				
Score obtained	70%	64%	72%	70%
Average score[1]	5.8	6.0	5.9	5.8
Goal	≥ 5	≥ 5	≥ 5	≥ 5
% ≥ Fruit/Vegetable goal[1]	68%	72%	70%	66%
Grain servings				
Score obtained	70%	64%	72%	70%
Average score[1]	5.6	5.5	5.5	5.6
Goal	≥ 6	≥ 6	≥ 6	≥ 6
% ≥ Grain goal[1]	35%	33%	33%	35%

[1] Of participants providing a score

Table 5.4c (continued)
Intervention Program Adherence Summary
Maintenance Sessions

	Maintenance Session - Year 3			
	Spring	**Summer**	**Fall**	**Winter**
Participants Assigned	2232	2728	1093	1548
Attendance	58%	53%	58%	54%
Completion	77%	69%	76%	77%
Self-Monitoring				
Fat Gram				
Score obtained	61%	52%	66%	63%
Average score[1]	27.8	27.4	26.9	28.2
Average goal	32.1	32.2	31.2	31.7
% ≤ Fat Gram goal[1]	78%	80%	77%	75%
Fruit/Vegetable servings				
Score obtained	61%	52%	66%	63%
Average score[1]	6.1	6.1	6.2	5.9
Goal	≥ 5	≥ 5	≥ 5	≥ 5
% ≥ Fruit/Vegetable goal[1]	76%	77%	76%	71%
Grain servings				
Score obtained	61%	52%	66%	63%
Average score[1]	5.8	5.6	5.7	5.7
Goal	≥ 6	≥ 6	≥ 6	≥ 6
% ≥ Grain goal[1]	39%	37%	38%	38%

[1] Of participants providing a score

Table 5.4c (continued)
Intervention Program Adherence Summary
Maintenance Sessions

	Maintenance Session - Year 4			
	Spring	**Summer**	**Fall**	**Winter**
Participants Assigned	56	359	-	-
Attendance	70%	49%	-	-
Completion	79%	59%	-	-
Self-Monitoring				
Fat Gram				
Score obtained	60%	43%	-	-
Average score[1]	29.6	26.6	-	-
Average goal	31.0	30.9	-	-
% ≤ Fat Gram goal[1]	62%	79%		
Fruit/Vegetable servings			-	-
Score obtained	60%	43%	-	-
Average score[1]	5.8	6.3	-	-
Goal	≥ 5	≥ 5		
% ≥ Fruit/Vegetable goal[1]	68%	84%		
Grain servings				
Score obtained	60%	43%	-	-
Average score[1]	5.6	5.8	-	-
Goal	≥ 6	≥ 6	-	-
% ≥ Grain goal[1]	38%	41%		

[1] Of participants providing a score

Table 5.4c (continued)
Intervention Program Adherence Summary
Maintenance Sessions

Participants with Revised (Lower) Fat Gram Goals

	Maintenance Session - Year 2			
	Spring	**Summer**	**Fall**	**Winter**
Participants Assigned	2131	3139	181	945
Attendance	65%	59%	64%	67%
Completion	81%	72%	86%	86%
Self-Monitoring				
Fat Gram				
Score obtained	68%	57%	72%	72%
Average score[1]	23.0	23.1	22.6	23.3
Average goal	24.6	24.6	24.6	24.6
% ≤ Fat Gram goal[1]	67%	67%	70%	62%
Fruit/Vegetable servings				
Score obtained	68%	57%	72%	72%
Average score[1]	5.7	5.9	5.6	5.6
Goal	≥ 5	≥ 5	≥ 5	≥ 5
% ≥ Fruit/Vegetable goal[1]	68%	71%	62%	63%
Grain servings				
Score obtained	68%	57%	72%	72%
Average score[1]	5.5	5.4	5.4	5.4
Goal	≥ 6	≥ 6	≥ 6	≥ 6
% ≥ Grain goal[1]	32%	32%	27%	32%

[1] Of participants providing a score

Table 5.5a
Body Weight

Body Weight (kg)[1]	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[2]	SE	p-value
All Participants									
Baseline	15887	76.7	16.5	23829	76.6	16.5	-0.1	0.2	0.61
Year 1	8946	73.9	16.1	13066	75.7	15.8	1.7	0.2	0.00
Year 2	3922	74.8	16.8	5788	75.7	15.9	0.9	0.3	0.01
Year 3	1181	74.3	16.1	1800	75.1	16.1	0.8	0.6	0.19
Minority Participants									
Baseline	2893	80.0	18.6	4258	79.6	18.8	-0.4	0.5	0.33
Year 1	1449	78.9	19.3	2052	78.9	18.6	0.0	0.6	0.95
Year 2	508	80.8	19.9	744	79.6	17.9	-1.2	1.1	0.28
Year 3	119	79.8	17.4	165	77.4	17.3	-2.4	2.1	0.25
Participants Aged 70-79									
Baseline	2463	72.6	14.3	3702	72.8	14.4	0.2	0.4	0.58
Year 1	1222	69.4	13.7	1823	71.6	14.1	2.1	0.5	0.00
Year 2	532	69.8	14.9	787	71.8	14.5	2.0	0.8	0.01
Year 3	139	69.4	13.5	225	70.6	14.2	1.2	1.5	0.42
Participants with Revised Fat Gram Goals[3]									
Baseline	12172	76.9	16.9	18288	76.9	17.0	0.0	0.2	0.96
Year 1	5481	74.3	16.7	8008	76.0	16.3	1.7	0.3	0.00
Year 2	677	75.4	18.7	1008	76.2	16.7	0.8	0.9	0.38

[1] Shown for 31.75 ≤ weight (kg) ≤ 226.8

[2] Control – Intervention.

[3] For revised fat gram goals: Intervention group is defined as women randomized to Intervention after 6/15/95 that have revised fat gram goals. Control group is defined as women randomized to Control after 6/15/95.

Table 5.6
Adherence to Follow-up Contacts

	Due	Conducted		Conducted in window	
	N	N	%	N	%
Semi-Annual Contact 1	31755	30228	95.2%	22539	71.0%
Intervention	12709	12130	95.4%	9073	71.4%
Control	19046	18098	95.0%	13466	70.7%
Annual Visit 1	23845	22435	94.1%	17625	73.9%
Intervention	9530	9071	95.2%	7220	75.8%
Control	14315	13364	93.4%	10405	72.7%
Semi-Annual Contact 2	16610	14876	89.6%	11107	66.9%
Intervention	6659	5965	89.6%	4445	66.8%
Control	9951	8911	89.5%	6662	66.9%
Annual Visit 2	10903	10007	91.8%	7514	68.9%
Intervention	4372	4030	92.2%	3055	69.9%
Control	6531	5977	91.5%	4459	68.3%
Semi-Annual Contact 3	6707	6015	89.7%	4234	63.1%
Intervention	2690	2419	89.9%	1696	63.0%
Control	4017	3596	89.5%	2538	63.2%
Annual Visit 3	3320	2951	88.9%	2391	72.0%
Intervention	1322	1173	88.7%	939	71.0%
Control	1998	1778	89.0%	1452	72.7%
Semi-Annual Contact 4	261	194	74.3%	157	60.2%
Intervention	100	72	72.0%	58	58.0%
Control	161	122	75.8%	99	61.5%

Table 5.7
Reasons for Stopping DM Intervention

Reasons[1]	(N = 325)[2]
Personal	105 (32%)
Travel	27 (8%)
Study Procedures	23 (7%)
Health	54 (17%)
Experiencing Health problems or symptom's not due to Intervention	46 (14%)
Worried about health effects of medical tests	1 (<1%)
Worried about costs if adverse effects occur	0 (0%)
Advised not to participate by health care provider	9 (3%)
Study conflicts with health care needs	6 (2%)
Expected more care	2 (1%)
Intervention	77 (24%)
Reports health problems or symptoms from WHI intervention	14 (4%)
Problem with Clinic Practitioner or other CC staff	1 (<1%)
Doesn't like taking pills	1 (<1%)
Doesn't like DM requirements	54 (17%)
Problems with DM group Nutritionist or Group members	7 (2%)
Doesn't like DM eating patterns	29 (9%)
Doesn't like randomized nature of intervention	2 (1%)
Expected some benefit from intervention	5 (2%)
Won't participate in safety procedures.	0 (0%)
Other	102 (31%)
Not Given	57 (18%)

[1] Multiple reasons may be reported for a woman

[2] Equals 2.0% of DM Intervention Participants

Table 5.8a
Selected Percentiles for Key Nutrients Based on FFQ Data from AV-1

	5%	10%	50%	90%	95%
Intervention					
% Energy from Fat	14.2	15.9	23.4	34.4	38.2
Total Energy (kcal)	743	883	1437	2133	2381
Total Fat (g)	16.6	19.9	36.6	65.8	78.6
Saturated Fat (g)	5.3	6.5	12.4	23.3	27.8
Polyunsaturated Fat (g)	3.1	3.7	6.7	12.7	15.6
Total Monosaturated Fat (g)	5.9	7.1	13.6	25.1	30.0
Calcium FFQ (mg)	271	347	707	1364	1600
Total Calcium (mg)	316	412	976	2075	2474
Iron (mg)	5.9	7.2	12.8	21.9	26.0
Fiber (g)	7.3	9.0	16.8	27.0	30.2
Protein (g)	29.8	36.4	63.7	100.0	114.0
Control					
% Energy from Fat	24.2	26.9	35.7	44.4	47.0
Total Energy (kcal)	739	871	1501	2377	2718
Total Fat (g)	24.7	30.4	58.3	102.5	121.2
Saturated Fat (g)	8.0	10.0	20.2	37.3	44.2
Polyunsaturated Fat (g)	4.4	5.5	11.1	20.9	24.7
Total Monosaturated Fat (g)	9.1	11.3	22.0	39.1	46.3
Calcium FFQ (mg)	240	304	635	1227	1457
Total Calcium (mg)	287	369	882	1965	2408
Iron (mg)	5.2	6.3	11.4	19.9	23.4
Fiber (g)	6.0	7.2	13.5	22.3	25.5
Protein (g)	28.9	35.0	63.0	102.1	116.4

Table 5.8a (continued)

Selected Percentiles for Key Nutrients Based on FFQ Data from AV-1

	5%	10%	50%	90%	95%
Intervention					
Carbohydrates (g)	100.9	120.7	207.1	315.2	353.5
Alcohol (g)	0.0	0.0	0.8	13.3	18.4
Vitamin A (mcg)	444.8	566.8	1114.7	1996.1	2338.0
Beta-carotene (mcg RE)	1365.1	1744.9	3881.4	8065.0	9690.9
Retinol (mcg RE)	110.3	152.6	402.6	859.0	1045.4
Vitamin C (mg)	44.3	57.3	123.9	210.1	239.2
Soluble Fiber	2.5	3.0	5.7	9.0	10.2
Alpha Toc (mg)	2.8	3.3	5.5	10.6	13.6
Vitamin D (mcg)	1.1	1.5	3.8	8.5	10.1
Cholesterol (mg)	58.2	73.9	147.7	276.1	332.1
Selenium (mcg)	42.2	51.6	92.7	147.9	167.3
Insoluble Fiber	4.7	5.8	11.0	17.9	20.1
Control					
Carbohydrates (g)	82.6	99.9	176.9	278.1	320.0
Alcohol (g)	0.0	0.0	0.8	13.2	18.7
Vitamin A (mcg)	421.1	520.7	1008.5	1821.4	2145.5
Beta-carotene (mcg RE)	1139.5	1487.6	3213.4	6847.6	8428.7
Retinol (mcg RE)	122.3	166.9	418.3	860.0	1039.4
Vitamin C (mg)	32.9	42.3	96.3	173.5	202.1
Soluble Fiber	2.1	2.5	4.6	7.5	8.6
Alpha Toc (mg)	3.1	3.8	6.9	12.4	15.0
Vitamin D (mcg)	1.2	1.6	4.0	8.4	10.2
Cholesterol (mg)	79.4	99.2	200.4	378.1	453.8
Selenium (mcg)	40.5	49.6	89.1	144.5	166.3
Insoluble Fiber	3.8	4.6	8.8	14.8	17.0

Table 5.8b

Selected Percentiles for Key Nutrients Based on FFQ Data from AV-1
For Women with Revised Fat Gram Goals

	5%	10%	50%	90%	95%
Intervention[1]					
% Energy from Fat	14.1	15.8	23.3	34.5	38.3
Total Energy (kcal)	740	881	1433	2125	2373
Total Fat (g)	16.7	19.9	36.3	65.3	78.1
Saturated Fat (g)	5.3	6.4	12.2	23.0	27.6
Polyunsaturated Fat (g)	3.1	3.7	6.6	12.3	15.3
Total Monosaturated Fat (g)	6.1	7.3	13.8	25.3	30.5
Calcium FFQ (mg)	273	348	710	1366	1611
Total Calcium (mg)	318	418	987	2126	2520
Iron (mg)	5.9	7.2	13.2	23.7	27.6
Fiber (g)	7.4	9.2	17.3	27.4	30.5
Protein (g)	29.9	36.0	62.8	99.4	113.2
Control[2]					
% Energy from Fat	24.7	27.3	35.8	44.5	46.9
Total Energy (kcal)	751	886	1507	2389	2736
Total Fat (g)	25.7	31.1	58.9	103.3	123.3
Saturated Fat (g)	8.2	10.2	20.3	37.5	45.1
Polyunsaturated Fat (g)	4.5	5.6	11.1	20.6	24.6
Total Monosaturated Fat (g)	9.5	11.8	22.5	40.1	47.8
Calcium FFQ (mg)	247	308	642	1242	1476
Total Calcium (mg)	296	377	925	2026	2501
Iron (mg)	5.3	6.3	11.9	21.1	25.1
Fiber (g)	6.2	7.5	14.0	22.9	26.0
Protein (g)	28.9	35.1	63.4	102.4	116.3

[1] Intervention group is defined as women randomized to Intervention after 6/15/95 that have revised fat gram goals.

[2] Control group is defined as women randomized to Control after 6/15/95.

Table 5.8b (continued)

Selected Percentiles for Key Nutrients Based on FFQ Data from AV-1
For Women with Revised Fat Gram Goals

	5%	10%	50%	90%	95%
Intervention[1]					
Carbohydrates (g)	101.0	120.4	206.6	313.5	352.2
Alcohol (g)	0.0	0.0	1.0	13.7	19.2
Vitamin A (mcg)	448.1	560.3	1113.4	1987.1	2328.2
Beta-carotene (mcg RE)	1387.4	1749.3	3934.2	8239.7	9778.6
Retinol (mcg RE)	107.3	149.2	387.5	833.4	1033.0
Vitamin C (mg)	45.6	58.3	124.9	210.9	241.0
Soluble Fiber	2.5	3.1	5.7	9.0	10.2
Alpha Toc (mg)	2.9	3.4	5.7	10.7	13.8
Vitamin D (mcg)	1.2	1.6	3.8	8.5	10.1
Cholesterol (mg)	57.2	72.7	146.1	273.1	326.5
Selenium (mcg)	41.3	50.2	90.0	141.9	160.8
Insoluble Fiber	4.8	6.0	11.3	18.5	20.6
Control[2]					
Carbohydrates (g)	83.3	100.2	177.5	278.4	321.8
Alcohol (g)	0.0	0.0	0.9	13.8	19.2
Vitamin A (mcg)	431.9	529.8	1017.1	1831.1	2169.0
Beta-carotene (mcg RE)	1159.8	1510.4	3275.7	6962.3	8550.3
Retinol (mcg RE)	125.4	167.3	415.5	859.2	1039.0
Vitamin C (mg)	33.3	43.3	96.7	175.0	202.7
Soluble Fiber	2.1	2.6	4.7	7.6	8.7
Alpha Toc (mg)	3.3	3.9	7.1	12.6	15.2
Vitamin D (mcg)	1.3	1.7	4.1	8.6	10.4
Cholesterol (mg)	80.3	100.5	202.3	382.5	455.4
Selenium (mcg)	40.3	49.2	88.5	143.1	164.0
Insoluble Fiber	3.9	4.8	9.2	15.3	17.4

[1] Intervention group is defined as women randomized to Intervention after 6/15/95 that have revised fat gram goals.

[2] Control group is defined as women randomized to Control after 6/15/95.

Table 5.9a
Body Weight Changes for Baseline - AV1 Weight Difference in Pounds[1]

	Lost ≥ 10 lbs		Lost < 10 lbs		Gained < 10 lbs		Gained ≥ 10 lbs		Totals	
	N	%	N	%	N	%	N	%	N	%
All participants										
Intervention										
BMI										
≤ 22.0	73	9.7	473	62.6	173	22.9	37	4.9	756	(8.5)
22.1 - 27.0	684	22.2	1660	53.9	638	20.7	97	3.2	3079	(34.6)
27.1 - 32.0	816	28.9	1326	47.0	581	20.6	98	3.5	2821	(31.7)
32.1 +	763	34.0	936	41.7	453	20.2	94	4.2	2246	(25.2)
	2336	26.2	4395	49.4	1845	20.7	326	3.7	8902	(100%)
Control										
BMI										
≤ 22.0	19	1.6	519	44.9	556	48.1	62	5.4	1156	(8.9)
22.1 - 27.0	231	5.1	1979	43.8	2075	46.0	230	5.1	4515	(34.8)
27.1 - 32.0	435	10.6	1691	41.3	1704	41.7	261	6.4	4091	(31.5)
32.1 +	522	16.2	1269	39.4	1173	36.4	259	8.0	3223	(24.8)
	1207	9.3	5458	42.0	5508	42.4	812	6.3	12985	(100%)
Minority Participants										
Intervention										
BMI										
≤ 22.0	3	4.0	51	67.1	19	25.0	3	4.0	76	(5.3)
22.1 - 27.0	51	13.8	202	54.6	97	26.2	20	5.4	370	(25.8)
27.1 - 32.0	85	18.5	233	50.8	116	25.3	25	5.5	459	(32.1)
32.1 +	105	19.9	241	45.7	145	27.5	36	6.8	527	(36.8)
	244	17.0	727	50.8	377	26.3	84	5.9	1432	(100%)
Control										
BMI										
≤ 22.0	5	3.8	60	45.8	61	46.6	5	3.8	131	(6.4)
22.1 - 27.0	26	4.9	229	43.0	246	46.2	32	6.0	533	(26.3)
27.1 - 32.0	60	9.0	277	41.5	287	43.0	43	6.5	667	(32.9)
32.1 +	98	14.0	281	40.3	261	37.4	58	8.3	698	(34.4)
	189	9.3	847	41.8	855	42.1	138	6.8	2029	(100%)

[1] Shown for 70 ≤ weight (lb) ≤ 500 and for weight differences < 70 lbs.

Table 5.9a (continued)
Body Weight Changes for Baseline - AV1 Weight Difference in Pounds[1]

	Lost ≥ 10 lbs		Lost < 10 lbs		Gained < 10 lbs		Gained ≥ 10 lbs		Totals	
	N	%	N	%	N	%	N	%	N	%
Participants Aged 70 - 79										
Intervention										
BMI										
≤ 22.0	11	8.7	77	60.6	36	28.4	3	2.4	127	(10.4)
22.1 - 27.0	96	22.2	256	59.3	71	16.4	9	2.1	432	(35.5)
27.1 - 32.0	115	27.9	216	52.4	73	17.7	8	1.9	412	(33.8)
32.1 +	86	34.8	122	49.4	33	13.4	6	2.4	247	(20.3)
	308	25.3	671	55.1	213	17.5	26	2.1	1218	(100%)
Control										
BMI										
≤ 22.0	1	0.7	83	53.6	67	43.2	4	2.6	155	(8.5)
22.1 - 27.0	38	5.5	335	48.8	292	42.6	21	3.1	686	(37.9)
27.1 - 32.0	61	9.7	294	46.5	253	40.0	24	3.8	632	(34.9)
32.1 +	45	13.3	160	47.2	120	35.4	14	4.1	339	(18.7)
	145	8.0	872	48.1	732	40.4	63	3.5	1812	(100%)

[1] Shown for 70 ≤ weight (lb) ≤ 500 and for weight differences < 70 lbs.

Table 5.9b
Body Weight Changes for Baseline - AV1 Weight Difference in Pounds[1]

	Lost >=10 lbs					Gained >= 10 lbs				
	5%	10%	50%	90%	95%	5%	10%	50%	90%	95%
All participants										
Intervention										
BMI										
≤ 22.0	10.4	10.6	12.8	19.6	22.0	10.1	10.4	16.1	25.4	49.4
22.1 - 27.0	10.4	10.8	13.9	21.4	25.4	10.6	10.8	15.0	29.8	38.8
27.1 - 32.0	10.4	10.8	14.6	25.8	30.0	10.4	10.6	15.3	30.6	39.5
32.1 +	10.8	11.2	17.2	32.6	38.8	10.4	11.0	13.9	23.1	28.4
Control										
BMI										
≤ 22.0	10.6	11.0	13.4	26.2	28.4	10.8	11.0	16.2	26.7	30.2
22.1 - 27.0	10.4	10.6	13.2	20.5	24.3	10.4	10.9	14.6	27.8	35.5
27.1 - 32.0	10.4	10.8	15.0	27.6	32.6	10.4	10.6	13.4	24.3	32.0
32.1 +	10.8	11.0	16.3	34.4	44.1	10.4	10.6	13.4	25.1	30.0
Minority Participants										
Intervention										
BMI										
≤ 22.0	12.1	12.1	13.4	16.8	16.8	10.1	10.1	11.5	21.2	21.2
22.1 - 27.0	10.4	11.0	13.7	20.7	36.2	10.3	10.5	15.9	27.6	34.0
27.1 - 32.0	10.6	10.6	13.2	23.8	25.8	10.6	10.6	13.0	26.0	30.9
32.1 +	10.6	11.0	16.1	30.9	37.7	10.1	10.4	13.7	23.1	43.7
Control										
BMI										
≤ 22.0	10.6	10.6	18.7	26.2	26.2	13.7	13.7	16.5	45.2	45.2
22.1 - 27.0	10.1	10.4	13.4	19.4	22.0	11.0	11.2	16.8	41.9	43.4
27.1 - 32.0	10.3	10.5	15.0	23.6	26.0	10.6	11.2	15.4	28.7	32.0
32.1 +	10.6	11.0	15.4	31.7	38.4	10.4	10.6	13.7	20.3	35.9

[1] Shown for 70 <= weight (lb) <= 500 and for weight differences < 70 lbs.

Table 5.7b (continued)
Body Weight Changes for Baseline - AV1 Weight Difference in Pounds[1]

	Lost >=10 lbs					Gained >= 10 lbs				
	5%	10%	50%	90%	95%	5%	10%	50%	90%	95%
Participants Aged 70 - 79										
Intervention										
BMI										
≤ 22.0	10.4	11.0	12.1	13.2	26.7	11.0	11.0	16.5	58.9	58.9
22.1 - 27.0	10.4	10.6	12.6	17.9	22.0	10.6	10.6	14.8	45.2	45.2
27.1 - 32.0	10.8	11.0	14.8	22.7	26.0	10.6	10.6	16.2	28.2	28.2
32.1 +	10.8	11.2	16.0	26.0	33.1	11.2	11.2	14.4	20.9	20.9
Control										
BMI										
≤ 22.0	28.4	28.4	28.4	28.4	28.4	13.4	13.4	22.4	45.2	45.2
22.1 - 27.0	10.4	10.6	14.0	20.1	26.0	11.9	12.1	19.0	35.5	36.8
27.1 - 32.0	10.6	10.8	13.4	20.5	22.9	10.6	11.0	14.9	40.6	41.9
32.1 +	10.8	11.0	14.6	35.3	37.9	10.1	10.4	13.8	26.9	29.8

[1] Shown for 70 <= weight (lb) <= 500 and for weight differences < 70 lbs.

6. CaD Intervention Status

6.1. Adherence to Supplements

The protocol calls for CT women to be offered CaD randomization at AV-1. A few exceptions are allowed to offer randomization at other times because of logistical constraints. To simplify the displays, women randomized at other times have been excluded from the adherence summaries. Originally, a clinic visit was required 6 months post-CaD randomization and adherence was assessed. Lower than anticipated adherence rates motivated a change in the follow-up procedures for CaD. A phone contact at four weeks post-CaD randomization was instituted to assist women in working through any potential problems they might be experiencing on CaD. To absorb this additional activity without increasing the cost of the study, the visit required at 6 months post-CaD randomization has been relaxed to be in the form of a visit or a telephone contact at clinic discretion. With this change, estimates of the six-month adherence rate become less reliable.

Table 6.1 presents rates of follow-up, stopping intervention and pill collection, and adherence to pill taking by visit schedule. The adherence pattern among women with pill collections is constant over time. The adherence summary, defined as those women known to be consuming 80% or more of the prescribed dose, is about 50%. This low adherence is a function of a significant proportion of women stopping the intervention entirely and lower than expected pill-taking rates among women staying on the intervention.

Table 6.2 summarizes interval and cumulative drop-out rates in comparison to the original design assumptions. The original power calculations for CaD assumed a 6% drop-out rate in year 1 and a 3% per year drop-out rate thereafter. An independent loss to follow-up rate of 3% per year was also incorporated resulting in approximately 8.8% stopping intervention in year 1 and 5.9% in subsequent years. Our current data suggest the drop-out rates are roughly twice the assumed level.

Since significant proportions of still active women are taking less than the prescribed dose, it is anticipated that this would have an additional effect on study power beyond drop-out rates. To examine these effects, we have calculated the power for CaD using the adherence model employed for the DM component. This approach incorporates total calcium intake from diet and supplements. To make within-model comparisons, we determined the calcium intake assumptions that would reproduce the original power calculations based on a model that dichotomized adherence to pills, holding constant all other parameters (e.g. treatment effect, lag time, control group incidence rates, and average follow-up time). Total calcium consumption (in mg) of 920, 950, 1000 at baseline, year 1 and year 9, respectively in controls and similarly 1920 in the intervention arm produces powers within 1%-2% of the protocol-specified values with n=45,000 for all outcomes of interest. The value of 920 mg/day in controls at baseline was determined from the median total calcium intake in the CaD participants at AV-1 who are also DM participants, thus providing FFQ data.

Table 6.3 describes the range of adherence patterns we examined. Using the adherence pattern suggested in *Table 6.1*, and anticipating that the new formulation will alleviate the poor adherence related to the size and taste of the tablets, we assume that a "moderate" adherence pattern may be achievable. Current adherence data are more suggestive of the "poor" scenario. *Table 6.4* shows the power for Hip Fractures, Other Fractures and colorectal cancer under three possible sample sizes

(45,000, 40,000, and 35,000) and all other parameters held constant. NB: Power is low for hip fracture and colo-rectal cancer in scenarios based on poor adherence or sample size <45,000. Power for all clinical fractures is adequate under most scenarios, especially if moderate adherence is achieved.

To understand factors related to adherence, we performed multivariate analyses of study subject characteristics using two measures of adherence calculated at SAV-2 and again at AV-2: the adherence summary value (1=known to be taking ≥ 80% of pills; 0 otherwise); and stopping CaD (1=stopping, 0=continuing). *Tables 6.5* through *6.8* present the fitted models. These analyses are consistent in indicating that increasing age is associated with better adherence while DM only participants and racial/ethnic minorities have lower adherence. The introduction of the 4-week call has had a modest but statistically significant effect towards improving adherence.

Table 6.9 summarizes the frequency of reported reasons for stopping CaD. The majority of women stopping study supplements do so of their own accord. Only 5% have indicated that they were advised by their physician to discontinue these supplements. Fifty-one percent of the women who have stopped taking their study pills report a reason related to the intervention itself, 17% report health reasons and 5% report personal reasons. Symptoms or health problem associated with the intervention was the most frequently reported intervention-related reason followed by dislike of the pills.

6.2. Issues

Previous efforts indicated that the chewable tablet formulation was a significant barrier to adherence. The tablet manufacturer has recently provided us with a swallowable tablet (OSCal), to offer as an alternative. The active version will contain 500 mg calcium carbonate and 125 IU vitamin D. This represents a small reduction in vitamin D dose, from 400 IU to 250 IU daily, but we consider this a reasonable substitute because this formulation and its placebo already exist and have Investigational New Drug (IND) approval with FDA. The manufacturer has agreed to develop a swallowable formulation with the original vitamin D levels, which we will use as soon as it becomes available.

With the two forms now available (in October 1997), women are given the choice of the chewable or swallowable forms, at randomization and at each follow-up dispensing. The database will track each woman's choice at each time point to support secondary analyses of dose and formulation, as appropriate. Effects on randomization rates should be evident in a few weeks time. Reliable estimates of the effect on adherence will not be available for another year.

Table 6.1
CaD Adherence Summary

	Due	Conducted		Conducted in Window		Stopped CaD		Missed Pill Collection		Total with Collections		Medication Rate[1] <50%		Medication Rate[1] 50%-80%		Medication Rate[1] 80% +		Adherence Summary[2]
	N	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	%
Semi-Annual Visit-2	10109	9605	95	7628	75	906	9.0	1780	18	8326	82	1439	17	1898	23	4989	60	49
Annual Visit-2	6034	5768	96	4477	74	411	6.8	652	12	4632	88	719	16	982	21	2931	63	49
Annual Visit -3	1964	1839	94	1505	77	253	12.9	332	19	1453	81	219	15	339	23	895	62	46

[1] Medication rate calculated as the number of pills taken divided by the number of days since bottle(s) were dispensed.

[2] Adherence summary calculated as the number of women consuming ≥80% of pills divided by the number due for a visit.

Note: Deceased women are excluded from all medication adherence calculations.

Table 6.2
CaD Drop-Out Rates (%) by Follow-Up Time
(Design-specified values in parentheses)

	Total	
	Interval[1]	Cumulative[2]
Drop-Outs[3]		
AV-2	15.1 (8.8)	15.1 (8.8)
AV-3	12.9 (5.9)	26.1 (14.2)

[1] Estimates of stopping or starting hormones in the Interval
[2] Estimates of cumulative rates
[3] Drop-out rates derived from Form 7 by date. Cumulative rates calculated as life-table estimates.

Table 6.3
Adherence Patterns used for Sensitivity Analyses

Adherence Pattern	Total Calcium Intake (mg)		
	Control	Intervention	Δ
Design[1]			
Baseline	920[2]	1920	1000
Year 1	950	1850	900
Year 9	1000	1800	800
Moderate Adherence			
Baseline	920	1920	1000
Year 1	930	1530	600
Year 9	950	1400	450
Poor Adherence			
Baseline	920	1920	1000
Year 1	930	1420	500
Year 9	950	1300	350

[1] Original power calculations had the same adherence assumptions as in HRT (i.e., 6% drop-out in Year 1, 3% per year thereafter, 1.5% per year drop-in plus 3% per year lost to follow-up in both arms). These total calcium intake assumptions produce approximately the same power for all designated endpoint in the total intake model.

[2] Median total calcium intake among CaD participants (with FFQs) at AV-1 (time of CaD randomization).

Table 6.4
Sensitivity of CaD Study Power to Adherence Assumptions
Design Sample Size of 45,000

	Year	Intervention Effect[1] (%)	Percentage of Cases[1]		Power under Various Calcium Intake Assumptions[2]		
			Control	Intervention	Design	Moderate	Poor
Hip Fractures							
	2001	18	1.52	1.27	68	31	22
		22	1.51	1.20	85	43	30
		25	1.49	1.13	95	56	39
	2004	18	2.68	2.19	92	47	32
		22	2.65	2.05	99	63	44
		25	2.62	1.92	>99	80	57
Combined Fractures							
	2001	18	6.13	5.18	>99	79	61
		22	6.07	4.92	>99	92	78
		25	6.01	4.66	>99	98	97
	2004	18	9.69	8.07	>99	92	75
		22	9.59	7.63	>99	98	89
		25	9.50	7.18	>99	>99	97
Colorectal Cancer							
	2001	18	0.80	0.69	30	15	12
		20	0.79	0.68	36	17	13
		22	0.78	0.66	42	20	15
	2004	18	1.32	1.06	84	42	30
		20	1.30	1.02	91	50	36
		22	1.29	0.98	96	58	42

[1] Intervention Effects and Percentage of Cases are shown for original Design assumptions. The other adherence patterns would produce greater incidence rates in Intervention women and a corresponding reduction in the estimated treatment effect.

[2] See Table 6.3 for corresponding adherence assumptions.

Table 6.4 (continued)
Sensitivity of CaD Study Power to Adherence Assumptions
Revised Sample Size of 40,000

	Year	Intervention Effect[1] (%)	Percentage of Cases[1]		Power under Various Calcium Intake Assumptions[2]		
			Control	Intervention	Design	Moderate	Poor
Hip Fractures							
	2001	18	1.52	1.27	63	28	20
		22	1.51	1.20	80	39	27
		25	1.49	1.13	92	51	36
	2004	18	2.68	2.19	89	43	29
		22	2.65	2.05	97	58	40
		25	2.62	1.92	>99	73	52
Combined Fractures							
	2001	18	6.13	5.18	99	75	56
		22	6.07	4.92	>99	89	73
		25	6.01	4.66	>99	97	86
	2004	18	9.69	8.07	>99	88	70
		22	9.59	7.63	>99	97	86
		25	9.50	7.18	>99	>99	95
Colorectal Cancer							
	2001	18	0.80	0.69	27	14	11
		20	0.79	0.68	33	16	12
		22	0.78	0.66	39	18	14
	2004	18	1.32	1.06	80	39	27
		20	1.30	1.02	88	46	32
		22	1.29	0.98	93	53	38

[1] Intervention Effects and Percentage of Cases are shown for original Design assumptions. The other adherence patterns would produce greater incidence rates in Intervention women and a corresponding reduction in the estimated treatment effect.

[2] See Table 6.3 for corresponding adherence assumptions.

Table 6.4 (continued)
Sensitivity of CaD Study Power to Adherence Assumptions
Revised Sample Size of 35,000

	Year	Intervention Effect[1] (%)	Percentage of Cases[1]		Power under Various Calcium Intake Assumptions[2]		
			Control	Intervention	Design	Moderate	Poor
Hip Fractures							
	2001	18	1.52	1.27	57	25	18
		22	1.51	1.20	75	35	24
		25	1.49	1.13	88	46	32
	2004	18	2.68	2.19	84	38	26
		22	2.65	2.05	95	53	36
		25	2.62	1.92	99	67	47
Combined Fractures							
	2001	18	6.13	5.18	98	69	51
		22	6.07	4.92	>99	85	68
		25	6.01	4.66	>99	94	82
	2004	18	9.69	8.07	>99	84	64
		22	9.59	7.63	>99	95	81
		25	9.50	7.18	>99	99	92
Colorectal Cancer							
	2001	18	0.80	0.69	25	13	10
		20	0.79	0.68	29	14	11
		22	0.78	0.66	34	17	13
	2004	18	1.32	1.06	74	34	24
		20	1.30	1.02	83	41	29
		22	1.29	0.98	90	48	34

[1] Intervention Effects and Percentage of Cases are shown for original Design assumptions. The other adherence patterns would produce greater incidence rates in Intervention women and a corresponding reduction in the estimated treatment effect.

[2] See Table 6.3 for corresponding adherence assumptions.

Table 6.5
Logistic Regression Analyses of CaD Adherence at Semi-Annual Vist-2 (SAV-2)
Data as of: 8/31/97

	CaD (n=10106)			
	Non-Adherent Participants (n=5117)	**Adherent[1] Participants (n=4989)**	**OR**	**95% C.I. For OR[2]**
Primary CT Randomization:				
DM and HRT[3]	623	838	1.00	
HRT only	1075	1555	1.05	(0.92,1.2)
DM only	3419	2596	.55**	(0.49,0.62)
Age:				
50-54	1196	895	1.00	
55-59	1387	1243	1.19**	(1.06,1.34)
60-69	1885	2099	1.41**	(1.26,1.58)
70-79	649	752	1.45**	(1.26,1.68)
Ethnicity:				
White	4216	4404	1.00	
Black	583	330	.59**	(0.5,0.68)
Hispanic	195	140	.66**	(0.52,0.85)
Other Minority	115	111	0.94	(0.72,1.24)
Education:				
Post H.S.	3975	3782	1.00	
Some H.S. / Diploma	1052	1113	1.04	(0.93,1.15)
0-8 Years	64	66	1.13	(0.77,1.66)
Income:				
<20 K	933	895	1.00	
20-35K	1211	1292	1.12	(0.98,1.27)
35K-50K	1063	1055	1.08	(0.94,1.24)
>50K	1820	1636	1.08	(0.94,1.23)
Marital Status:				
Married	3247	3224	1.00	
Not Married	1852	1746	0.96	(0.87,1.05)
Four Week Phone Call[4]:				
No	1091	970	1.00	
Yes	1023	1133	1.15*	(1.02,1.31)

[1] Defined as taking 80% or more of their study pills. Participants with missing pill collections are considered non-adherent (adherence=0).

[2] Assuming asymptotic normality for parameter estimates.

[3] Underlined levels are reference categories.

[4] Includes participants randomized to CaD after 8/15/96.

*P-values <=.05 from Wald Test.

**P-values <=.01 from Wald Test.

Table 6.6
Logistic Regression Analyses of Stopping CaD by Semi-Annual Visit-2 (SAV-2)
Data as of: 8/31/97

	CaD (n=10106)			
	Active Participants (n=9200)	Inactive[1] Participants (n=906)	Odds Ratio for Stopping	95% C.I. For OR[2]
Primary CT Randomization:				
DM and HRT[3]	1372	89	1.00	
HRT only	2446	184	1.18	(0.9,1.53)
DM only	5382	633	1.86**	(1.47,2.35)
Age:				
50-54	1897	194	1.00	
55-59	2409	221	0.93	(0.75,1.14)
60-69	3628	356	1.00	(0.83,1.21)
70-79	1266	135	1.14	(0.89,1.46)
Ethnicity:				
White	7838	782	1.00	
Black	838	75	0.88	(0.67,1.14)
Hispanic	309	26	0.93	(0.6,1.44)
Other Minority	205	21	1.08	(0.68,1.71)
Education:				
Post H.S.	7038	719	1.00	
Some H.S. / Diploma	1991	174	0.90	(0.75,1.08)
0-8 Years	120	10	0.89	(0.45,1.77)
Income:				
<20 K	1668	160	1.00	
20-35K	2294	209	0.93	(0.74,1.16)
35K-50K	1919	199	1.04	(0.83,1.32)
>50K	3132	324	0.98	(0.77,1.23)
Marital Status:				
Married	5891	580	1.00	
Not Married	3276	322	1.00	(0.85,1.18)
Four Week Phone Call[4]:				
No	1865	196	1.00	
Yes	1964	192	0.92	(0.74,1.14)

[1] Inactive defined as stopping CaD supplements between CaD randomization and SAV-2.

[2] Assuming asymptotic normality for parameter estimates.

[3] Underlined levels are reference categories.

[4] Includes participants randomized to CaD after 8/15/96.

*P-values <=.05 from Wald Test.

**P-values <=.01 from Wald Test.

Table 6.7
Logistic Regression Analyses of CaD Adherence at Annual Visit-2 (AV-2)
For Participants with >80% CaD Adherence at SAV-2
Data as of: 8/31/97

	CaD (n=2918)			
	Non-Adherent Participants (n=711)	**Adherent[1] Participants (n=2207)**	**OR**	**95% C.I. For OR[2]**
Primary CT Randomization:				
DM and HRT[3]	93	431	1.00	
HRT only	164	667	0.88	(0.66,1.17)
DM only	454	1109	.53**	(0.41,0.69)
Age:				
50-54	138	369	1.00	
55-59	172	514	1.09	(0.83,1.43)
60-69	304	972	1.10	(0.86,1.41)
70-79	97	352	1.28	(0.93,1.76)
Ethnicity:				
White	603	2015	1.00	
Black	69	112	.48**	(0.34,0.69)
Hispanic	26	42	.55*	(0.31,0.96)
Other Minority	12	38	1.02	(0.52,2)
Education:				
Post H.S.	544	1639	1.00	
Some H.S. / Diploma	152	533	1.09	(0.88,1.36)
0-8 Years	14	23	0.62	(0.29,1.32)
Income:				
<20 K	124	411	1.00	
20-35K	187	607	0.94	(0.71,1.24)
35K-50K	143	472	0.93	(0.69,1.26)
>50K	233	679	0.84	(0.62,1.13)
Marital Status:				
Married	432	1451	1.00	
Not Married	278	749	.77*	(0.63,0.94)

[1] Defined as taking 80% or more of their study pills. Participants with missing pill collections are considered non-adherent (adherence=0).

[2] Assuming asymptotic normality for parameter estimates.

[3] Underlined levels are reference categories.

Table 6.8
Logistic Regression Analyses of Stopping CaD Between SAV-2 and AV2
For Participants Who Were Active in CaD at SAV-2
Data as of: 8/31/97

	CaD (n=5498)			
	Active Participants (n=5087)	Inactive[1] Participants (n=411)	Odds Ratio for Stopping	95% C.I. For OR[2]
Primary CT Randomization:				
DM and HRT[3]	807	54	1.00	
HRT only	1256	69	0.80	(0.55,1.16)
DM only	3024	288	1.43*	(1.05,1.95)
Age:				
50-54	1032	89	1.00	
55-59	1245	121	1.17	(0.88,1.56)
60-69	2099	144	0.91	(0.68,1.21)
70-79	711	57	1.09	(0.76,1.57)
Ethnicity:				
White	4408	355	1.00	
Black	441	43	1.09	(0.76,1.56)
Hispanic	140	11	0.98	(0.5,1.91)
Other Minority	94	2	0.26	(0.06,1.08)
Education:				
Post H.S.	3847	317	1.00	
Some H.S. / Diploma	1154	89	1.06	(0.81,1.37)
0-8 Years	63	5	1.07	(0.4,2.84)
Income:				
<20 K	923	64	1.00	
20-35K	1345	94	1.03	(0.73,1.44)
35K-50K	1052	95	1.29	(0.91,1.84)
>50K	1671	149	1.19	(0.83,1.7)
Marital Status:				
Married	3274	267	1.00	
Not Married	1798	144	1.06	(0.84,1.35)

[1] Inactive defined as stopping CaD supplements between SAV-2 and AV-2.

[2] Assuming asymptotic normality for parameter estimates.

[3] Underlined levels are reference categories.

Table 6.9
Reasons for Stopping CaD

Reasons[1]	(N = 1970)
Personal	89 (5%)
Travel	16 (1%)
Study Procedures	18 (1%)
Health	326 (17%)
Experiencing Health problems or symptom's not due to Intervention	194 (10%)
Worried about health effects of medical tests	5 (<1%)
Worried about costs if adverse effects occur	5 (<1%)
Advised not to participate by health care provider	95 (5%)
Study conflicts with health care needs	64 (3%)
Expected more care	6 (<1%)
Intervention	1101 (51%)
Reports health problems or symptoms from WHI intervention	656 (33%)
Problem with Clinic Practitioner or other CC staff	2 (<1%)
Doesn't like taking pills	333 (17%)
Doesn't like DM requirements	3 (<1%)
Problems with DM group Nutritionist or Group members	1 (<1%)
Doesn't like DM eating patterns	1 (<1%)
Doesn't like randomized nature of intervention	75 (4%)
Expected some benefit from intervention	13 (1%)
Won't participate in safety procedures.	3 (<1%)
Other	629 (32%)
Not Given	236 (12%)

[1] Multiple reasons may be reported for a woman.

7. OS Activities

7.1. Overview of Follow-up

OS follow-up is conducted by annual mailed self-administered questionnaires except for year 3. Approximately 2 months prior to the anniversary of the participants enrollment, the CCC mails the Medical History Update and the OS Exposure Update questionnaires. Participants mail their completed questionnaires to their local CC for data entry and outcomes processing. Non-respondents receive up to two additional mailings from the CCC. For odd numbered follow-up years, CCs must attempt to complete follow-up of non-responders by local contacts, usually telephone reminders or interviews.

The year 3 clinic visit was incorporated to assess change in physical measures, blood analytes, diet use of medications and supplements. These visits are scheduled to begin in the first VCCs in Fall, 1997.

7.2. Completeness of Follow-up

Table 7.1 shows completeness of OS follow-up by follow-up year, type of contact and clinic group. These rates reflect our experience with those participants for whom the sequence of mailings are complete and there has been at least two months for CC follow-up. Though these rates are generally good, they do not yet meet the goal of 95% complete at year 1 and 94% at year 2.

Table 7.1
Response rates to OS Follow-up Procedures

		Mailings Initiated[1]		Response to Mailings		Response to CC follow-up		Total Responses	
	# Due	N	%	N	%	N	% [2]	N	%
Year 1	32378	32080	99.1%	27207	84.8%	2143	44.0%	29350	91.5%
VCC	16196	16154	99.7%	13735	85.0%	1158	47.9%	14893	92.2%
NCC	16182	15926	98.4%	13472	84.6%	985	40.1%	14457	90.8%
Year 2	5514	5320	96.5%	4779	89.8%	2	0.4%	4781	89.9%
VCC	4772	4603	96.5%	4159	90.4%	2	0.5%	4161	90.4%
NCC	742	717	96.6%	620	86.5%	0	0.0%	620	86.5%

[1] Mailings are not sent to women who have requested no follow-up, who are deceased, or who have a non-deliverable address at the time of first contact.

[2] Percentage of OS participants not responding to mailings. CC follow-up not required in even numbered follow-up years.

8. Intermediate Outcomes

8.1 Blood Specimen Analysis

WHI assesses intermediate effects of interventions through analyses of stored blood samples on a small subsample of CT participants at baseline and years 1, 3, 6 and 9. This subsample is stratified by study component (HRT vs. DM), Clinical Center and by race with oversampling of minorities. To reduce the variability that could arise from laboratory drift, baseline and year one samples are paired and sent to the laboratory in the same batch. The laboratory is blinded to all participant information.

Table 8.1 shows the mean values of all routine blood analytes at baseline and AV-1, the changes over time and the differences between HRT participants with and without a uterus. To make these results more representative of the accrued population, weighted averages and standard errors of the ethnic-specific results are presented with the weights defined as the proportion currently enrolled in each racial/ethnic category (Whites, Blacks, Hispanics, and Other). The only significant differences ($p < 0.01$) in change from baseline between the groups defined by uterine strata are in HDL-C and HDL-3 where the increase is greater in hysterectomized women than in those without a uterus.

For reference, published results of the the PEPI study[1] are summarized below showing the mean changes at three years of follow-up (from baseline) for selected outcomes with the corresponding WHI results at one year. PEPI did not stratify by hysterectomy status so they report results for a single placebo arm.

	PEPI 3 year results			Current WHI 1 year results	
	ERT	PERT	Placebo	Without Uterus	With Uterus
Fibrinogen (mg/dl)	-20[1]	1[1]	10[1]	-8.6	-2.0
HDL-C (mg/dl)	5.6	1.2	-1.2	5.4	2.6
LDL-C (mg/dl)	-14.5	-16.5	-4.1	-15.1	-12.6
Total cholesterol (mg/dl)	-7.6	-14.0	-4.2	-8.8	-10.3
Triglycerides (mg/dl)	13.7[1]	11.4[1]	-3.2[1]	4.5	-2.1
Glucose (mg/dl)	-2.8	-2.1	-0.5	-5.4	-2.5
Insulin (uIU/ml)	-.24[1]	-.53[1]	.53[1]	-0.8	-0.4

[1] Calculated on log-transformed values.

For completeness, *Table 8.2* displays the same analytes measured in DM women. For comparison purposes, the Women's Health Trial: Feasibility Study in Minority Populations have reported

[1] The Writing Group for the PEPI Trial. Effects of Estrogen or Estrogen/Progestin Regimens on Heart Disease Risk Factors in Postmenopausal Women. JAMA (1995) 273(3):199-208)

dietary intake and changes in total cholesterol.[1] The results at baseline and approximately 12 months post-randomization are summarized below with the corresponding WHI results.

	WHT:FSMP Results		
	Intervention	Control	C-I
FFQ % cal from fat			
Baseline	39.7	39.1	-0.6
12 months	25.7	36.0	10.3
Total cholesterol (mg/dl)			
Baseline	219	219	0
Change at 12 months	-8.4	-4.9	-3.5

Prospective analyses of OS bloods for these routine measures will be conducted for participants in the OS Measurement Precision Study. These data are not yet available.

8.2 Bone Mineral Density

Bone scans are given to all enrolled WHI participants in three Clinical Centers: Birmingham, Pittsburgh and Tucson. The choice of three centers was based on reducing the variability associated with multiple sites and operators while achieving adequate sample size. The selection of these three Clinical Centers was based both on their previous experience in bone densitometry and the expected enrollment of minorities which will allow us to address hypotheses regarding racial/ethnic differences.

Tables 8.3 - 8.5 show for each study component specific BMD means and standard deviations for baseline, AV-1 and AV-3 along with change from baseline and percent bone loss for the three types of scans available: whole body, spine, and hip. The number of scans available at AV-3 is still small indicating that these estimates may be unstable.

Baseline values for the CaD component are a subset of the AV-1 results. The first follow-up bone scans after CaD randomization are obtained at AV-3.

[1] Coates RJ, Bowen DJ, Kristal AR, et al. The Women's Health Trial Feasibility Study in Minority Populations: changes in dietary intakes. Unpublished manuscript

Table 8.1
Blood Specimen Analysis: HRT Participants
(Data as of: 8/31/97)

	With Uterus			Without Uterus		
	n	mean*	std.*	n	mean*	std.*
Micronutrients						
Alpha-Carotene (μg/ml)						
Baseline	147	0.09	0.07	123	0.08	0.09
AV-1	147	0.10	0.07	123	0.07	0.04
AV-1 - Baseline	147	0.01	0.05	123	-0.01	0.08
Alpha-tocopherol (μg/ml)						
Baseline	147	15.5	5.4	123	15.5	5.6
AV-1	147	15.6	5.4	123	17.0	6.2
AV-1 - Baseline	147	0.2	4.1	123	1.5	5.1
Beta-Carotene (μg/ml)						
Baseline	147	0.31	0.17	123	0.26	0.16
AV-1	147	0.28	0.23	123	0.23	0.28
AV-1 - Baseline	147	-0.03	0.15	123	-0.03	0.29
Beta-Cryptoxanthine (μg/ml)						
Baseline	147	0.08	0.06	123	0.07	0.04
AV-1	147	0.08	0.05	123	0.06	0.04
AV-1 - Baseline	147	0.00	0.05	123	-0.01	0.04
Gamma-tocopherol (μg/ml)						
Baseline	147	2.45	1.11	123	2.44	1.02
AV-1	147	1.97	0.95	123	2.22	1.19
AV-1 - Baseline	147	-0.48	0.86	123	-0.22	0.96
Lycopene (μg/ml)						
Baseline	147	0.40	0.17	123	0.38	0.15
AV-1	147	0.39	0.15	123	0.36	0.10
AV-1 - Baseline	147	-0.01	0.15	123	-0.01	0.11
Lutein and Zeaxanthin (μg/ml)						
Baseline	147	0.21	0.08	123	0.21	0.07
AV-1	147	0.22	0.08	123	0.21	0.07
AV-1 - Baseline	147	0.00	0.05	123	0.00	0.05
Retinol (μg/ml)						
Baseline	147	0.59	0.12	123	0.61	0.11
AV-1	147	0.60	0.11	123	0.62	0.12
AV-1 - Baseline	147	0.01	0.08	123	0.02	0.06

* Means and standard deviations are weighted by ethnicity using the ethnicity distribution of participants randomized to CT.

Table 8.1 (Continued)

	With Uterus			Without Uterus		
	n	mean*	std.*	n	mean*	std.*
Clotting Factor						
Factor VII Activity, Antigen (%)						
Baseline	147	113.2	24.5	122	121.2	19.3
AV-1	147	119.3	25.7	122	124.2	22.2
AV-1 – Baseline	147	6.1	16.9	121	3.6	13.7
Factor VII C (%)						
Baseline	147	129.6	37.6	122	161.3	118.3
AV-1	147	128.4	26.1	122	161.3	54.5
AV-1 – Baseline	147	-1.2	36.8	121	11.1	57.1
Fibrinogen (mg/dl)						
Baseline	147	309.0	49.7	122	321.1	53.0
AV-1	147	307.0	52.5	122	312.5	53.0
AV-1 – Baseline	147	-2.0	53.0	121	-8.6	42.5
Hormones / Other						
Glucose (mg/dl)						
Baseline	146	102.7	28.4	123	109.2	32.6
AV-1	147	100.1	21.4	123	103.9	24.9
AV-1 – Baseline	146	-2.5	15.3	123	-5.4	18.3
Insulin (μIU/ml)						
Baseline	146	10.9	4.4	122	13.2	6.4
AV-1	146	10.3	4.0	123	12.4	6.2
AV-1 – Baseline	145	-0.4	2.8	122	-0.8	3.8

* Means and standard deviations are weighted by ethnicity using the ethnicity distribution of participants randomized to CT.

Table 8.1 (Continued)

	With Uterus			Without Uterus		
	n	mean*	std.*	n	mean*	std.*
Lipoproteins						
HDL-2 (mg/dl)						
Baseline	138	16.0	7.0	120	15.1	6.6
AV-1	140	18.6	8.0	118	17.9	7.6
AV-1 – Baseline	133	2.0	3.8	115	2.8	3.9
HDL-3 (mg/dl)						
Baseline	138	40.5	6.5	120	39.7	6.3
AV-1	140	41.1	6.0	118	42.8	7.1
AV-1 – Baseline	133	0.4	4.5	115	2.6	4.8
HDL-C (mg/dl)						
Baseline	146	56.8	12.1	123	55.1	12.0
AV-1	146	59.7	12.0	123	60.5	12.7
AV-1 – Baseline	145	2.6	6.2	123	5.4	7.7
LDL-C (mg/dl)						
Baseline	142	140.2	29.2	122	143.5	32.1
AV-1	144	127.9	26.0	121	128.6	27.4
AV-1 – Baseline	141	-12.6	24.7	121	-15.1	24.0
Lp(a) (mg/dl)						
Baseline	145	25.6	21.2	122	23.5	18.0
AV-1	145	22.2	17.1	123	22.4	18.8
AV-1 – Baseline	143	-3.3	8.5	122	-1.2	6.6
Total Cholesterol (mg/dl)						
Baseline	146	228.6	34.4	123	231.5	31.8
AV-1	146	218.6	29.0	123	222.7	26.5
AV-1 – Baseline	145	-10.3	26.0	123	-8.8	24.3
Triglyceride (mg/dl)						
Baseline	146	155.1	71.6	123	165.8	60.4
AV-1	145	150.9	53.6	123	170.2	72.6
AV-1 – Baseline	144	-2.1	46.9	123	4.5	50.5

* Means and standard deviations are weighted by ethnicity using the ethnicity distribution of participants randomized to CT.

Table 8.2
Blood Specimen Analysis: DM Participants
(Data as of: 8/31/97)

	n	mean*	std.*
Micronutrients			
Alpha-Carotene (μg/ml)			
Baseline	404	0.09	0.06
AV-1	405	0.09	0.05
AV-1 – Baseline	404	0.00	0.06
Alpha-tocopherol (μg/ml)			
Baseline	404	15.6	5.4
AV-1	405	16.5	5.5
AV-1 – Baseline	404	0.8	3.9
Beta-Carotene (μg/ml)			
Baseline	404	0.28	0.19
AV-1	405	0.28	0.21
AV-1 – Baseline	404	0.00	0.19
Beta-Cryptoxanthine (μg/ml)			
Baseline	404	0.08	0.04
AV-1	405	0.08	0.04
AV-1 – Baseline	404	0.00	0.04
Gamma-tocopherol (μg/ml)			
Baseline	404	2.28	1.16
AV-1	405	1.90	1.03
AV-1 – Baseline	404	-0.39	0.84
Lycopene (μg/ml)			
Baseline	404	0.41	0.15
AV-1	405	0.41	0.15
AV-1 – Baseline	404	0.00	0.13
Lutein and Zeaxanthin (μg/ml)			
Baseline	404	0.23	0.09
AV-1	405	0.23	0.08
AV-1 – Baseline	404	0.00	0.06
Retinol (μg/ml)			
Baseline	404	0.62	0.12
AV-1	405	0.62	0.13
AV-1 – Baseline	404	0.00	0.08

* Means and standard deviations are weighted by ethnicity using the ethnicity distribution of participants randomized to CT.

Table 8.2 (Continued)

	n	mean*	std.*
Clotting Factors			
Factor VII Activity, Antigen (%)			
Baseline	404	121.9	25.1
AV-1	400	121.3	25.5
AV-1 - Baseline	399	-0.5	15.7
Factor VII C (%)			
Baseline	404	147.4	54.7
AV-1	400	153.3	103.0
AV-1 - Baseline	399	3.8	106.9
Fibrinogen (mg/dl)			
Baseline	404	299.7	47.9
AV-1	400	298.9	49.1
AV-1 - Baseline	399	-0.5	38.1
Hormones/Other			
Glucose (mg/dl)			
Baseline	405	99.4	21.0
AV-1	405	97.9	20.4
AV-1 - Baseline	405	-1.5	16.9
Insulin (μIU/ml)			
Baseline	402	10.9	5.0
AV-1	404	11.2	13.8
AV-1 - Baseline	401	0.4	12.4

* Means and standard deviations are weighted by ethnicity using the ethnicity distribution of participants randomized to CT.

Table 8.2 (Continued)

	n	mean*	std.*
Lipoproteins			
HDL-2 (mg/dl)			
Baseline	392	17.5	7.2
AV-1	394	18.0	7.0
AV-1 - Baseline	385	0.5	4.3
HDL-3 (mg/dl)			
Baseline	392	42.5	7.3
AV-1	394	41.4	6.5
AV-1 - Baseline	385	-1.1	4.5
HDL-C (mg/dl)			
Baseline	404	60.0	13.0
AV-1	404	59.6	11.7
AV-1 - Baseline	403	-0.5	6.8
LDL-C (mg/dl)			
Baseline	399	136.6	28.4
AV-1	397	130.3	28.1
AV-1 - Baseline	394	-6.1	18.8
Lp(a) (mg/dl)			
Baseline	398	26.7	25.6
AV-1	402	27.3	26.9
AV-1 - Baseline	396	0.1	9.0
Total Cholesterol (mg/dl)			
Baseline	405	228.6	33.4
AV-1	404	222.0	30.5
AV-1 - Baseline	404	-6.7	22.0
Triglyceride (mg/dl)			
Baseline	405	156.6	66.1
AV-1	404	159.3	63.5
AV-1 - Baseline	404	2.7	44.0

* Means and standard deviations are weighted by ethnicity using the ethnicity distribution of participants randomized to CT.

Table 8.3
Bone Mineral Density Analysis: HRT Participants
Data as of: 8/31/97

	With Uterus			Without Uterus		
	n	mean	std.	n	mean	std.
Whole Body Scan						
Baseline	936	0.99	0.10	864	1.01	0.10
AV1	522	1.00	0.10	496	1.01	0.11
AV3	115	1.01	0.11	92	1.02	0.12
AV1 % Change in baseline BMD[1]	519	0.03	2.49	493	0.23	2.66
AV3 % Change in baseline BMD[2]	115	1.84	2.98	91	1.31	3.30
Spine Scan						
Baseline	917	0.95	0.16	844	0.97	0.16
AV1	508	0.97	0.16	491	0.99	0.16
AV3	112	0.99	0.18	91	0.99	0.18
AV1 % Change in baseline BMD	505	1.82	4.23	489	1.74	4.79
AV3 % Change in baseline BMD	112	4.44	5.25	91	2.60	5.99
Hip Scan						
Baseline	934	0.84	0.13	861	0.86	0.14
AV1	521	0.85	0.14	496	0.87	0.14
AV3	115	0.86	0.13	90	0.89	0.16
AV1 % Change in baseline BMD	519	0.65	3.02	493	0.61	3.11
AV3 % Change in baseline BMD	115	2.72	4.47	90	2.58	4.34

[1] AV1 % Change in baseline BMD is defined as ((AV1-Baseline)/Baseline)x100
[2] AV3 % Change in baseline BMD is defined as ((AV3-Baseline)/Baseline)x100

Table 8.4
Bone Mineral Density Analysis: DM Participants
Data as of: 8/31/97

	n	mean	std.
Whole Body Scan			
Baseline	3558	1.03	0.11
AV1	2532	1.03	0.11
AV3	415	1.04	0.11
AV1 % Change in baseline BMD[1]	2506	0.06	2.50
AV3 % Change in baseline BMD[2]	411	1.05	3.09
Spine Scan			
Baseline	3497	0.99	0.17
AV1	2492	0.99	0.17
AV3	405	1.00	0.17
AV1 % Change in baseline BMD	2475	0.69	3.81
AV3 % Change in baseline BMD	403	2.08	4.91
Hip Scan			
Baseline	3558	0.87	0.14
AV1	2532	0.87	0.14
AV3	412	0.89	0.14
AV1 % Change in baseline BMD	2519	-0.05	2.81
AV3 % Change in baseline BMD	410	1.66	3.91

[1] AV1 % Change in baseline BMD is defined as ((AV1-Baseline)/Baseline)x100
[2] AV3 % Change in baseline BMD is defined as ((AV3-Baseline)/Baseline)x100

Table 8.5
Bone Mineral Density Analysis: CaD Participants
Data as of: 8/31/97

	n	mean	std.
Whole Body Scan			
AV1	1600	1.02	0.10
AV3	283	1.03	0.11
AV3 % Change in baseline BMD[1]	279	1.66	2.60
Spine Scan			
AV1	1570	0.99	0.16
AV3	279	1.00	0.16
AV3 % Change in baseline BMD[1]	274	2.15	4.20
Hip Scan			
AV1	1597	0.87	0.14
AV3	281	0.88	0.14
AV3 % Change in baseline BMD[1]	277	2.47	3.11

[1]Percent Change in BMD is defined as ((AV3-AV1)/AV1)x100

9. Outcomes

9.1 Overview

Most outcomes are initially ascertained by self-report on Form 33 - Medical History Update. CT participants complete this form every six months, OS participants complete this form every year. Those participants who report an outcome requiring documentation and adjudication are asked to complete a more detailed form (Form 33D) that collects the information needed to request the associated medical records. After these forms are completed and entered into the database, the CCs execute a database function that identifies adjudication cases based on the Form 33D information. CCs then request hospital and related records as specified in Volume 8 - Outcomes for each outcome category. Once the cases are documented, clinic staff send the charts to the local physician adjudicator for evaluation and classification. Upon return, clinic staff enter the local determinations into the WHI database. Key cardiovascular outcomes are adjudicated by a central committee process. Currently WHI requires central adjudication of all such events, though the intent is to move to central adjudication on a sampling basis when satisfactory agreement has been reached between the local and central processes. The investigators at UCSF subcontract to the CCC (Steve Cummings, PI) to adjudicate all hip fractures. Staff at the CCC code and adjudicate all cancers of major interest in the study (breast, colon, rectum, ovary, and endometrium) using standardized SEER-type guidelines.

We present data both for self-reported and locally adjudicated outcomes. The monitoring analysis are conducted on outcomes as classified by the local adjudicator, however. Central adjudication results, while offering a higher degree of standardization, will eventually be available only on a subsample, and even then only after a lag time of several months. The central adjudication process should therefore be viewed primarily as a quality assurance effort.

9.2 Outcomes Data Quality

Table 9.1 - Timeliness and Completeness of Local Adjudication displays the distribution of time required to locally adjudicate a self-reported outcome by month of Form 33. This table is based on the day on which form was completed, which may not be the same as the day on which the form was entered in the database. Thus, some of the more recent data will improve when more adjudications are entered in the database. Overall 70% of self-reported outcomes in the CT and OS requiring adjudication have been locally adjudicated, 26% within 90 days of self-report and 44% within 180 days. More recently CCs have completed 46% of the local processing within 90 days, and about 70% within 180 days. Completion rates differ for different outcome types (see *Table 9.3* and its discussion below) for reasons that are related to the amount of documentation required for each outcome.

The outcomes ascertainment, documentation and adjudication effort is by necessity a lengthy process involving interaction between the clinical center and the participant and her health care providers. Delays in obtaining these data are attributable to problems in acquiring a participant's medical record, as well as local adjudicator and clinical processing issues. The experience before the middle of 1996 represents performance during the time when outcome procedures were not fully formulated or implemented. The entire process is more mature now, and many of the sources of delay are being or have been addressed.

Some of the biggest hurdles, however, are related to the interactions with the providers and these will continue to slow the outcomes process, particularly when the event of interest occurred near to the time of the participant's self-report. In these instances the chart may not be complete or available, causing clinics to need to issue multiple requests.

Table 9.2 - Agreement of Local Adjudications with Self-Reports shows the condition types that the participant can indicate on Form 33 or Form 33D and estimates of the chance that the local adjudicator agrees with that condition. Because of the complications of the adjudication process, it is hard to come up with an accurate estimate of the accuracy of self-reports. For example, for most outcome types second events do not need to be adjudicated, but if the participant reports a second outcome before the first outcome is confirmed, an adjudication case will be opened. This case should be closed when the first outcome is confirmed. Some self-reports get combined into one adjudication case. Except in rare circumstances though, the first self-report of a particular outcome will be adjudicated. Therefore, only first self-reports were used for *Table 9.2*. Since a few self-reports may have been combined with self-reports for other outcomes on the same Form 33, we consider an outcome confirmed if the adjudicator agrees with that outcome on any of the adjudication cases resulting from the same Form 33D.

As can be seen from this table, the accuracy of self-reports varies considerably by outcome. In particular, the accuracy of cancer self-reports is considerably higher than the accuracy of fractures and cardiovascular self-reports. The accuracy of self-reports of Angina, PVD, DVT, and PE is thus far less than 50%.

Table 9.3 - Number of Cases Resulting from Self-Reports shows the progress of the adjudication process by outcome. In this table all self-reports of a particular outcome by a participant are considered. Thus, the data underlying this table is slightly different from the data underlying *Table 9.2*, which only used the first self-report of each outcome. As can be seen from this table, there is some difference in the fraction of open adjudications between different outcomes: about 40% of the participants with a cancer report still have an open adjudication, while only about 30% of the participants with a cardiovascular or fracture report have an open adjudication. This table, in combination with *Table 9.2*, also allows for an estimate of the total number of cases that will result from the current self-reports.

Table 9.4 - Agreement of Central Adjudications with Local Adjudications shows that there is good agreement between local and central adjudications for all outcomes except Angina and Congestive Heart Failure. Approximately 140 more cardiovascular outcomes are scheduled to be adjudicated at the October 1997 annual meeting. Some self-reports are locally adjudicated as one type of outcome, while they are centrally adjudicated as another outcome. Since we see the central adjudication process primarily as quality assurance, data regarding such cross classification is not shown.

9.3 Outcomes overview

Tables 9.5--9.9 Counts (Annualized Percentages) of Participants with Self-Reported Outcomes for the Clinical trial, Dietary Modification Component, Hormone Replacement Therapy Component, Calcium and Vitamin D Component, and Observational Study, contains counts of the number of self-reports for the major WHI outcomes. Note that for many of the outcomes

the participants over-report (see *Tables 9.2-9.4*), so the numbers in these tables should be seen as upper bounds to the number of outcomes that currently have occurred.

For the DM, HRT and CaD tables, the counts and rates are based on all the participants in the control arm(s) and the intervention arm(s). Because of the blinding of the study, we cannot provide information about the number of participants in separate arms.

It is interesting to notice that the participant in the Observational Study have a considerably lower annualized rate of ever being hospitalized than the Clinical Trial participants (6.10% versus 8.63%). For most outcomes the CT participants seem to have slightly higher rates than the OS participants, but the difference between the two rates is typically much lower than the difference for hospitalizations.

Currently we are observing higher rates of breast cancer than of MI in both the CT and the OS. We expect that this will change over time, since there likely is a considerably larger ``healthy volunteer effect'' for MI than for breast cancer. This healthy volunteer effect should diminish over time.

Tables 9.10--9.14 Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for the Clinical trial, Dietary Modification Component, Hormone Replacement Therapy Component, Calcium and Vitamin D Component, and Observational Study, contains the same information as *Tables 9.5* through *9.9*, but for the locally verified outcomes, rather than self-reports. Since a number of the outcomes still needs to be adjudicated, the numbers in these tables give a lower bound on the number of outcomes that currently have occurred. When we get further in the study, hopefully the number of not yet adjudicated cases will decrease as a fraction of the total number of cases, at which stage these tables may give more accurate information than *Tables 9.5-9.9*.

Tables 9.15 Counts (Annualized Percentages) of Locally Verified Outcomes for HRT participants With and Without Uterus compares all participants with a uterus (PERT and placebo arm) with all participants without a uterus (ERT and placebo arm). A Z-value based upon a weighted log-rank test is provided. The log-rank test that we used is the same as the one being used to compare treatments, as specified in the study protocol. We here summarize the essential details about these weighted log-rank tests.

- The weighting is intended to enhance test power. The weights are chosen to vary linearly from 0 at time of randomization to 1 at a disease-specific maximum (three years for cardiovascular events and fracture occurrence, ten years for cancer occurrence and total mortality), and to be constant there after.

- The tests are stratified on baseline self-reported prevalent disease (if applicable) and baseline age (50--54, 55--59, 60--69, 70--79) and for the HRT trial on hysterectomy status. The strata for participants without prevalent disease are further stratified on participation in the other studies. The strata for participants with prevalent disease are not further stratified, since the resulting strata would be so small, that test-efficiency would be lost.

- For ``other cancer'' and ``other fracture'' only the first other cancer (any type) and other fracture (any type) are used for computing the log-rank statistic.

When examining the Z-values in these tables one should keep in mind that since we are looking at 21 test statistics at the same time, a multiple testing correction on significance level would have to be made. A Bonferroni correction would put the 2-sided 5% Z-value at 3.04 and the 2-sided 1% Z-value at 3.49. It thus appears that most of the effects are on the noise level, possibly with the exception of DVT and PE, which appear to occur more often in women with a uterus.

Table 9.1
Timeliness and Completeness of Local Adjudications - CT and OS

Forms with conditions[1]		Number and % of forms with conditions locally adjudicated by days from Form 33 encounter date to completion of local adjudication											
Date of Form 33 encounter		≤ 90		91 - 120		121 - 150		151 - 180		> 180		Not yet adjudicated	
	N	N	%	N	%	N	%	N	%	N	%	N	%
≤ May 31 1996	3568	241	7%	130	4%	167	5%	191	5%	2405	67%	434	12%
1996 June	317	92	29%	27	9%	19	6%	25	8%	113	36%	41	13%
1996 July	354	86	24%	37	10%	36	10%	37	10%	115	32%	43	12%
1996 August	437	94	22%	38	9%	40	9%	38	9%	156	36%	71	16%
1996 September	443	109	25%	52	12%	57	13%	34	8%	115	26%	76	17%
1996 October	532	128	24%	78	15%	53	10%	41	8%	126	24%	106	20%
1996 November	376	95	25%	57	15%	54	14%	40	11%	60	16%	70	19%
1996 December	467	145	31%	50	11%	63	13%	56	12%	53	11%	100	21%
1997 January	618	222	36%	88	14%	63	10%	28	5%	47	8%	170	28%
1997 February	527	187	35%	85	16%	41	8%	45	9%	15	3%	154	29%
1997 March	1487	687	46%	174	12%	86	6%	26	2%[2]			514	35%
1997 April	857	424	49%	103	12%	26	3%[2]					304	35%
1997 May	669	328	49%	43	6%[2]							298	45%
1997 June	804	276	34%[2]									528	66%
1997 July	616	94	15%[2]									522	85%
1997 August	342	15	4%[2]									327	96%
Total	12414	3223	26%	962	8%	705	6%	561	5%	3205	26%	3758	30%

[1] Conditions are self-reported events that require additional documentation.

[2] This table is based on the day the form was completed, not on the day the form was entered in the database. Thus, some of the more recent entries will still improve when more adjudications are entered in the database.

Table 9.2
Agreement of the Local Adjudications with Self-Reports - CT and OS

Outcomes	Number of participants with at least one self-report	Number of the first self-reports that have been adjudicated	Number of these adjudications that agree with the self-report	Percent agreement
Cardiovascular				
MI	188	116	79	68%
Angina	476	302	117	39%
Congestive heart failure	108	67	47	70%
CABG/PTCA	297	187	155	83%
Carotid artery disease	56	36	25	69%
Stroke	275	166	97	55%
PVD	55	33	14	42%
DVT	100	68	21	31%
PE	48	30	12	40%
Cancers				
Breast cancer	403	232	210	91%
Ovary cancer	41	24	16	67%
Endometrial cancer	55	31	27	87%
Colerectal	113	69	56	81%
Other (non-skin) cancer	478	292	183	63%
Fractures				
Hip fracture	69	44	29	66%
Other fracture	2112	1541	810	53%
Other				
Hysterectomy	27	11	11	100%
Death	133	82	82	100%

Note: a few first self-reports that were not adjudicated, for example because the report was combined with another self-report, have been excluded from this table.

Table 9.3
Number of Cases Resulting from Self-Reports - CT and OS

Outcomes	Number of participants with at least one self-report	Number of these participants with a confirmed outcome	Number of these participants for whom all self-reports are denied	Number of these participants with an open adjudication
Cardiovascular				
MI	188	80	35	73
Angina	476	128	174	174
Congestive heart failure	108	50	20	38
CABG/PTCA	297	161	27	109
Carotid artery disease	56	26	10	20
Stroke	275	93	73	109
PVD	55	15	18	22
DVT	100	23	45	32
PE	48	12	18	18
Cancers				
Breast cancer	403	216	17	170
Not in situ		178		
In situ		44		
Ovary cancer	41	16	8	17
Endometrial cancer	55	27	4	24
Colerectal	113	56	13	44
Other (non-skin) cancer	478	190	104	184
Fractures				
Hip fracture	69	29	15	25
Other fracture	2112	821	718	573
Vertebral		57		
Non vertebral		773		
Other				
Hysterectomy	27	11	0	16
Death	133	82	0	51

Note: for most outcomes later self-reports are not adjudicated if a participant has a confirmed outcome of that same outcome (which may be based upon a self-report for another outcome).

Table 9.4
Agreement of Central Adjudications with Local Adjudications - CT and OS

Outcomes	Number of locally confirmed cases	Number of these cases that have been centrally adjudicated	Number of these adjudications that agree with the local adjudication	Percent agreement
Cardiovascular				
MI[1]	129	43	40	93%
Angina[2]	246	72	54	75%
Congestive heart failure	105	33	23	70%
CABG/PTCA	187	52	47	99%
DVT[3]	28	10	10	100%
PE[3]	15	6	6	100%
Cancers				
Breast cancer	222	67	65	97%
Non in situ	176	47	46	98%
In situ	46	18	13	72%
Ovary cancer	20	3	3	100%
Endometrial cancer	35	8	7	88%
Colerectal	63	26	24	92%
Fractures				
Hip fracture	36	5	5	100%
Other				
Death	99	18	18	100%

[1] Of the 129 participants with a confirmed MI, 80 self-reported MI, 16 are based upon self-reports of Angina, 17 are based upon a self-report of another cardiovascular event, and 16 are based upon self-reports of a non-cardiovascular event.

[2] Of the 246 participants with a confirmed Angina, 129 participants self-reported Angina, 18 are based upon self-reports of MI, 44 are based upon a self-report of another cardiovascular event, and 55 are based upon self-reports of a non-cardiovascular event.

[3] DVT and PE are centrally adjudicated since May of 1997.

Table 9.5
Counts (Annualized Percentages) of Participants with Self-Reported Outcomes for Clinical Trial
Data as of: 08/31/97

	Total		Age 50-54		55-59		60-69		70-79		Ethnicity Minority[1]		White	
No. of participants w/ Form 33	42251		7883		10146		17267		6955		7376		34875	
Mean follow-up (months) [2]	17.0		17.8		17.3		16.9		16.0		15.5		17.3	
Outcomes														
Hospitalizations														
Ever	5167	(8.63%)	742	(6.35%)	968	(6.62%)	2340	(9.62%)	1117	(12.05%)	744	(7.81%)	4423	(8.80%)
Two or more	1604		197		283		727		397		210		1394	
Cardiovascular														
MI	125	(0.21%)	11	(0.09%)	14	(0.10%)	56	(0.23%)	44	(0.47%)	19	(0.20%)	106	(0.21%)
Angina	309	(0.52%)	28	(0.24%)	43	(0.29%)	139	(0.57%)	99	(1.07%)	62	(0.65%)	247	(0.49%)
Heart failure	60	(0.10%)	4	(0.03%)	7	(0.05%)	24	(0.10%)	25	(0.27%)	14	(0.15%)	46	(0.09%)
CABG/PTCA	198	(0.33%)	13	(0.11%)	34	(0.23%)	85	(0.35%)	66	(0.71%)	26	(0.27%)	172	(0.34%)
Carotid endarterectomy	35	(0.06%)	2	(0.02%)	3	(0.02%)	16	(0.07%)	14	(0.15%)	0	(0.00%)	35	(0.07%)
Stroke	163	(0.27%)	9	(0.08%)	16	(0.11%)	71	(0.29%)	67	(0.72%)	32	(0.34%)	131	(0.26%)
PVD	26	(0.04%)	3	(0.03%)	8	(0.05%)	12	(0.05%)	3	(0.03%)	4	(0.04%)	22	(0.04%))
DVT	95	(0.16%)	10	(0.09%)	16	(0.11%)	42	(0.17%)	27	(0.29%)	11	(0.12%)	84	(0.17%)
PE	43	(0.07%)	3	(0.03%)	8	(0.05%)	17	(0.07%)	15	(0.16%)	3	(0.03%)	40	(0.08%)
Cancer														
Breast cancer	205	(0.34%)	26	(0.22%)	47	(0.32%)	88	(0.36%)	44	(0.47%)	28	(0.29%)	177	(0.35%)
Ovary cancer	28	(0.05%)	5	(0.04%)	4	(0.03%)	15	(0.06%)	4	(0.04%)	2	(0.02%)	26	(0.05%)
Endometrial cancer [3]	30	(0.09%)	6	(0.09%)	5	(0.06%)	11	(0.08%)	8	(0.16%)	2	(0.04%)	28	(0.09%)
Colo-rectal cancer	73	(0.12%)	7	(0.06%)	12	(0.08%)	31	(0.13%)	23	(0.25%)	16	(0.17%)	57	(0.11%)
Other (non-skin) cancer [4]	276	(0.46%)	36	(0.31%)	49	(0.33%)	120	(0.49%)	71	(0.77%)	27	(0.28%)	249	(0.50%)

Table 9.9 (continued)
Counts (Annualized Percentages) of Participants with Self-Reported Outcomes for Observational Study
Data as of: 08/31/97

	Total		Age 50-54		55-59		60-69		70-79		Ethnicity Minority[1]		White	
Fractures														
Hip fracture	34	(0.06%)	1	(0.01%)	4	(0.04%)	14	(0.06%)	15	(0.13%)	1	(0.01%)	33	(0.07%)
Vertebral fracture	72	(0.13%)	5	(0.05%)	9	(0.08%)	29	(0.13%)	29	(0.26%)	4	(0.06%)	68	(0.15%)
Other fracture [4]	983	(1.84%)	137	(1.50%)	193	(1.69%)	415	(1.91%)	238	(2.10%)	84	(1.21%)	899	(1.93%)
Other														
Diabetes (treated)	1202	(2.24%)	125	(1.37%)	212	(1.86%)	544	(2.51%)	321	(2.83%)	378	(5.44%)	824	(1.77%)
Hysterectomy [3]	273	(0.87%)	63	(1.17%)	46	(0.64%)	105	(0.83%)	59	(0.94%)	46	(1.26%)	227	(0.82%)
Deaths	116	(0.22%)	8	(0.09%)	13	(0.11%)	45	(0.21%)	50	(0.44%)	18	(0.26%)	98	(0.21%)

[1] Participants with unmarked ethnicity are classified as minority.
[2] Mean follow-up is the number of months from enrollment to the last Form 33 or date of death from Form 124 (Final Report of Death).
[3] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer and hysterectomy.
[4] Only one report of "other cancer" or "other fracture" is reported; however, the first other cancer or other fracture of each type is adjudicated.

Table 9.10
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Clinical Trial
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
No. of participants w/ Form 33	42251		7883		10146		17267		6955		7376		34875	
Mean follow-up (months) [2]	17.0		17.8		17.3		16.9		16.0		15.5		17.3	
Outcomes														
Cardiovascular														
MI	89	(0.15%)	7	(0.06%)	8	(0.05%)	40	(0.16%)	34	(0.37%)	11	(0.12%)	78	(0.16%)
Sudden coronary death	11	(0.02%)	0	(0.00%)	2	(0.01%)	3	(0.01%)	6	(0.06%)	2	(0.02%)	9	(0.02%)
Angina	136	(0.23%)	11	(0.09%)	20	(0.14%)	62	(0.25%)	43	(0.46%)	24	(0.25%)	112	(0.22%)
Congestive heart failure	54	(0.09%)	2	(0.02%)	5	(0.03%)	23	(0.09%)	24	(0.26%)	9	(0.09%)	45	(0.09%)
CABG/PTCA	113	(0.19%)	9	(0.08%)	14	(0.10%)	46	(0.19%)	44	(0.47%)	14	(0.15%)	99	(0.20%)
Carotid artery disease	23	(0.04%)	2	0.02%)	4	(0.03%)	6	(0.02%)	11	(0.12%)	4	(0.04%)	19	(0.04%)
Stroke	64	(0.11%)	5	(0.04%)	3	(0.02%)	29	(0.12%)	27	(0.29%)	9	(0.09%)	55	(0.11%)
PVD	14	(0.02%)	0	(0.00%)	3	(0.02%)	6	(0.02%)	5	(0.05%)	5	(0.05%)	9	(0.02%)
DVT	24	(0.04%)	1	(0.01%)	1	(0.01%)	11	(0.05%)	11	(0.12%)	3	(0.03%)	21	(0.04%)
PE	12	(0.02%)	0	(0.00%)	2	(0.01%)	5	(0.02%)	5	(0.05%)	3	(0.03%)	9	(0.02%)
Cancer														
Breast cancer [3]	106	(0.18%)	7	(0.06%)	21	(0.14%)	50	(0.21%)	28	(0.30%)	12	(0.13%)	94	(0.19%)
Invasive breast cancer	84	(0.14%)	5	(0.04%)	17	(0.12%)	39	(0.16%)	23	(0.25%)	9	(0.09%)	75	(0.15%)
In situ breast cancer [4]	25	(0.04%)	2	(0.02%)	4	(0.03%)	12	(0.05%)	7	(0.08%)	3	(0.03%)	22	(0.04%)
Ovary cancer	12	(0.02%)	1	(0.01%)	3	(0.02%)	6	(0.02%)	2	(0.02%)	1	(0.01%)	11	(0.02%)
Endometrial cancer	16	(0.05%)	3	(0.05%)	1	(0.01%)	7	(0.05%)	5	(0.10%)	1	(0.02%)	15	(0.05%)
Colo-rectal cancer	37	(0.06%)	4	(0.03%)	4	(0.03%))	16	(0.07%)	13	(0.14%)	6	(0.06%)	31	(0.06%)
Other (non-skin) cancer [5]	130	(0.22%)	15	(0.13%)	21	(0.14%)	61	(0.25%)	33	(0.36%)	8	(0.08%)	122	(0.24%)

Table 9.10 (continued)
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Clinical Trial
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
Fractures														
Hip fracture	20	(0.03%)	1	(0.01%)	1	(0.01%)	4	(0.02%)	14	(0.15%)	1	(0.01%)	19	(0.04%)
Vertebral fracture	39	(0.07%)	3	(0.03%)	5	(0.03%)	16	(0.07%)	15	(0.16%)	1	(0.01%)	38	(0.08%)
Other fracture [5,6]	554	(0.93%)	99	(0.85%)	88	(0.60%)	260	(1.07%)	107	(1.15%)	45	(0.47%)	509	(1.01%)
Other														
Deaths	60	(0.10%)	4	(0.03%)	5	(0.03%)	32	(0.13%)	19	(0.20%)	8	(0.08%)	52	(0.10%)

[1] Participants with unmarked ethnicity are classified as minority.
[2] Mean follow-up is the number of months from enrollment to the last Form 33 or date of death from Form 124 (Final Report of Death).
[3] Excludes two cases with borderline malignancy.
[4] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.
[5] Only one report of "other cancer" or "other fracture" is reported; however, the first other cancer or other fracture of each type is adjudicated.
[6] "Other fracture" excludes fractures indicated as pathological.

Table 9.11
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Hormone Replacement Therapy Component
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
No. of participants w/ Form 33	15918		2769		3487		6602		3060		3005		12913	
Mean follow-up (months) [2]	16.4		16.6		16.5		16.7		15.3		15.2		16.6	
Outcomes														
Cardiovascular														
MI	39	(0.18%)	3	(0.08%)	4	(0.08%)	19	(0.21%)	13	(0.33%)	6	(0.16%)	33	(0.18%)
Sudden coronary death	6	(0.03%)	0	(0.00%)	1	(0.02%)	3	(0.03%)	2	(0.05%)	2	(0.05%)	4	(0.02%)
Angina	56	(0.26%)	2	(0.05%)	13	(0.27%)	26	(0.28%)	15	(0.38%)	11	(0.29%)	45	(0.25%)
Congestive heart failure	24	(0.11%)	0	(0.00%)	3	(0.06%)	11	(0.12%)	10	(0.26%)	5	(0.13%)	19	(0.11%)
CABG/PTCA	47	(0.22%)	2	(0.05%)	9	(0.19%)	20	(0.22%)	16	(0.41%)	7	(0.18%)	40	(0.22%)
Carotid artery disease	11	(0.05%)	0	(0.00%)	2	(0.04%)	3	(0.03%)	6	(0.15%)	1	(0.03%)	10	(0.06%)
Stroke	27	(0.12%)	1	(0.03%)	1	(0.02%)	10	(0.11%)	15	(0.38%)	4	(0.11%)	23	(0.13%)
PVD	6	(0.03%)	0	(0.00%)	3	(0.06%)	2	(0.02%)	1	(0.03%)	2	(0.05%)	4	(0.02%)
DVT	22	(0.10%)	1	(0.03%)	1	(0.02%)	10	(0.11%)	10	(0.26%)	3	(0.08%)	19	(0.11%)
PE	11	(0.05%)	0	(0.00%)	2	(0.04%)	5	(0.05%)	4	(0.10%)	3	(0.08%)	8	(0.04%)
Cancer														
Breast cancer	25	(0.11%)	1	(0.03%)	4	(0.08%)	10	(0.11%)	10	(0.26%)	1	(0.03%)	24	(0.13%)
Invasive breast cancer	18	(0.08%)	1	(0.03%)	3	(0.06%)	7	(0.08%)	7	(0.18%)	1	(0.03%)	17	(0.10%)
In situ breast cancer	7	(0.03%)	0	(0.00%)	1	(0.02%)	3	(0.03%)	3	(0.08%)	0	(0.00%)	7	(0.04%)
Ovary cancer	3	(0.01%)	0	(0.00%)	0	(0.00%)	3	(0.03%)	0	(0.00%)	0	(0.00%)	3	(0.02%)
Endometrial cancer [3]	2	(0.02%)	0	(0.00%)	0	(0.00%)	1	(0.02%)	1	(0.05%)	0	(0.00%)	2	(0.02%)
Colo-rectal cancer	16	(0.07%)	1	(0.03%)	0	(0.00%)	8	(0.09%)	7	(0.18%)	4	(0.11%)	12	(0.07%)
Other (non-skin) cancer [4]	53	(0.24%)	5	(0.13%)	8	(0.17%)	28	(0.30%)	12	(0.31%)	5	(0.13%)	48	(0.27%)

Table 9.11 (continued)
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Hormone Replacement Therapy Component
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
Fractures														
Hip fracture	5	(0.02%)	1	(0.03%)	0	(0.00%)	0	(0.00%)	4	(0.10%)	1	(0.03%)	4	(0.02%)
Vertebral fracture	13	(0.06%)	1	(0.03%)	5	(0.10%)	6	(0.07%)	1	(0.03%)	0	(0.00%)	13	(0.07%)
Other fracture [4,5]	215	(0.99%)	32	(0.84%)	24	(0.50%)	118	(1.28%)	41	(1.05%)	17	(0.45%)	198	(1.11%)
Other														
Hysterectomy [3]	31	(0.24%)	5	(0.22%)	4	(0.13%)	15	(0.27%)	7	(0.32%)	5	(0.27%)	26	(0.23%)
Deaths	25	(0.11%)	2	(0.05%)	3	(0.06%)	12	(0.13%)	8	(0.21%	3	(0.08%)	22	(0.12%)

[1] Participants with unmarked ethnicity are classified as minority.
[2] Mean follow-up is the number of months from enrollment to the last Form 33 or date of death from Form 124 (Final Report of Death).
[3] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer and hysterectomy.
[4] Only one report of "other cancer" or "other fracture" is reported; however, the first other cancer or other fracture of each type is adjudicated.
[5] "Other fracture" excludes fractures indicated as pathological.

Table 9.12
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Dietary Modification Component
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
No. of participants w/ Form 33	31514		6127		7887		12827		4673		5443		26071	
Mean follow-up (months) [2]	17.4		18.3		17.6		17.2		16.4		15.7		17.8	
Outcomes														
Cardiovascular														
MI	62	(0.14%)	4	(0.04%)	6	(0.05%)	28	(0.15%)	24	(0.38%)	6	(0.08%)	56	(0.14%)
Sudden coronary death	7	(0.02%)	0	(0.00%)	1	(0.01%)	2	(0.01%)	4	(0.06%)	0	(0.00%)	7	(0.02%)
Angina	94	(0.21%)	9	(0.10%)	8	(0.07%)	47	(0.26%)	30	(0.47%)	16	(0.22%)	78	(0.20%)
Congestive heart failure	39	(0.09%)	2	(0.02%)	3	(0.03%)	17	(0.09%)	17	(0.27%)	8	(0.11%)	31	(0.08%)
CABG/PTCA	76	(0.17%)	7	(0.07%)	8	(0.07%)	31	(0.17%)	30	(0.47%)	8	(0.11%)	68	(0.18%)
Carotid artery disease	14	(0.03%)	2	(0.02%)	2	(0.02%)	4	(0.02%)	6	(0.09%)	3	(0.04%)	11	(0.03%)
Stroke	47	(0.10%)	4	(0.04%)	3	(0.03%)	26	(0.14%)	14	(0.22%)	7	(0.10%)	40	(0.10%)
PVD	11	(0.02%)	0	(0.00%)	1	(0.01%)	5	(0.03%)	5	(0.08%)	4	(0.06%)	7	(0.02%)
DVT	11	(0.02%)	0	(0.00%)	0	(0.00%)	5	(0.03%)	6	(0.09%)	1	(0.01%)	10	(0.03%)
PE	3	(0.01%)	0	(0.00%)	0	(0.00%)	0	(0.00%)	3	(0.05%)	0	(0.00%)	3	(0.01%)
Cancer														
Breast cancer [3]	87	(0.19%)	6	(0.06%)	18	(0.16%)	43	(0.23%)	20	(0.31%)	11	(0.15%)	76	(0.20%)
Invasive breast cancer	72	(0.16%)	4	(0.04%)	15	(0.13%)	35	(0.19%)	18	(0.28%)	8	(0.11%)	64	(0.17%)
In situ breast cancer	18	(0.04%)	2	(0.02%)	3	(0.03%)	9	(0.05%)	4	(0.06%)	3	(0.04%)	15	(0.04%)
Ovary cancer	9	(0.02%)	1	(0.01%)	3	(0.03%)	3	(0.02%)	2	(0.03%)	1	(0.01%)	8	(0.02%)
Endometrial cancer [4]	15	(0.06%)	3	(0.06%)	1	(0.01%)	6	(0.06%)	5	(0.15%)	1	(0.03%)	14	(0.06%)
Colo-rectal cancer	24	(0.05%)	3	(0.03%)	4	(0.03%)	10	(0.05%)	7	(0.11%)	3	(0.04%)	21	(0.05%)
Other (non-skin) cancer [5]	98	(0.21%)	12	(0.13%)	18	(0.16%)	46	(0.25%)	22	(0.34%)	6	(0.08%)	92	(0.24%)

Table 9.12 (continued)
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Dietary Modification Component
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
Fractures														
Hip fracture	15	(0.03%)	0	(0.00%)	1	(0.01%)	4	(0.02%)	10	(0.16%)	0	(0.00%)	15	(0.04%)
Vertebral fracture	31	(0.07%)	3	(0.03%)	2	(0.02%)	12	(0.07%)	14	(0.22%)	1	(0.01%)	30	(0.08%)
Other fracture [5,6]	418	(0.91%)	79	(0.85%)	78	(0.67%)	188	(1.02%)	73	(1.14%)	34	(0.48%)	384	(0.99%)
Other														
Deaths	42	(0.09%)	3	(0.03%)	3	(0.03%)	22	(0.12%)	14	(0.22%)	5	(0.07%)	37	(0.10%)

[1] Participants with unmarked ethnicity are classified as minority.
[2] Mean follow-up is the number of months from enrollment to the last Form 33 or date of death from Form 124 (Final Report of Death).
[3] Excludes two cases with borderline malignancy.
[4] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.
[5] Only one report of "other cancer" or "other fracture" is reported; however, the first other cancer or other fracture of each type is adjudicated.
[6] "Other fracture" excludes fractures indicated as pathological.

Table 9.13
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Calcium and Vitamin D Component
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
No. of participants w/ Form 33	11176		2272		2881		4470		1553		1549		9627	
Mean follow-up (months) [2]	11.9		12.0		11.6		12.2		11.7		11.0		12.1	
Outcomes														
Cardiovascular														
MI	17	(0.15%)	1	(0.04%)	1	(0.04%)	9	(0.20%)	6	(0.40%)	0	(0.00%)	17	(0.18%)
Sudden coronary death	3	(0.03%)	0	(0.00%)	0	(0.00%)	1	(0.02%)	2	(0.13%)	0	(0.00%)	3	(0.03%)
Angina	23	(0.21%)	2	(0.09%)	3	(0.11%)	9	(0.20%)	9	(0.59%)	1	(0.07%)	22	(0.23%)
Congestive heart failure	5	(0.05%)	0	(0.00%)	1	(0.04%)	3	(0.07%)	1	(0.07%)	0	(0.00%)	5	(0.05%)
CABG/PTCA	21	(0.19%)	2	(0.09%)	3	(0.11%)	8	(0.18%)	8	(0.53%)	1	(0.07%)	20	(0.21%)
Carotid artery disease	5	(0.05%)	0	(0.00%)	2	(0.07%)	2	(0.04%)	1	(0.07%)	2	(0.14%)	3	(0.03%)
Stroke	11	(0.10%)	1	(0.04%)	1	(0.04%)	6	(0.13%)	3	(0.20%)	0	(0.00%)	11	(0.11%)
PVD	5	(0.05%)	0	(0.00%)	0	(0.00%)	1	(0.02%)	4	(0.26%)	1	(0.07%)	4	(0.04%)
DVT	4	(0.04%)	0	(0.00%)	0	(0.00%)	2	(0.04%)	2	(0.13%)	0	(0.00%)	4	(0.04%)
PE	0	(0.00%)	0	(0.00%)	0	(0.00%)	0	(0.00%)	0	(0.00%)	0	(0.00%)	0	(0.00%)
Cancer														
Breast cancer [3]	31	(0.28%)	2	(0.09%)	7	(0.25%)	15	(0.33%)	7	(0.46%)	2	(0.14%)	29	(0.30%)
Invasive breast cancer	24	(0.22%)	1	(0.04%)	7	(0.25%)	11	(0.24%)	5	(0.33%)	2	(0.14%)	22	(0.23%)
In situ breast cancer	7	(0.06%)	1	(0.04%)	0	(0.00%)	4	(0.09%)	2	(0.13%)	0	(0.00%)	7	(0.07%)
Ovary cancer	5	(0.05%)	0	(0.00%)	1	(0.04%)	3	(0.07%)	1	(0.07%)	0	(0.00%)	5	(0.05%)
Endometrial cancer [4]	2	(0.03%)	1	(0.08%)	0	(0.00%)	1	(0.04%)	0	(0.00%)	0	(0.00%)	2	(0.03%)
Colo-rectal cancer	7	(0.06%)	1	(0.04%)	1	(0.04%)	2	(0.04%)	3	(0.20%)	1	(0.07%)	6	(0.06%)
Other (non-skin) cancer [4]	25	(0.23%)	3	(0.13%)	4	(0.14%)	12	(0.26%	6	(0.40%)	2	(0.14%)	23	(0.24%)

Table 9.13 (continued)
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Calcium and Vitamin D Component
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
Fractures														
Hip fracture	2	(0.02%)	1	(0.04%)	0	(0.00%)	1	(0.02%)	0	(0.00%)	0	(0.00%)	2	(0.02%)
Vertebral fracture	4	(0.04%)	0	(0.00%)	1	(0.04%)	2	(0.04%)	1	(0.07%)	0	(0.00%)	4	(0.04%)
Other fracture [5,6]	74	(0.67%)	16	(0.71%)	7	(0.25%)	33	(0.73%)	18	(1.19%)	4	(0.28%)	70	(0.72%)
Other														
Deaths	9	(0.08%)	1	(0.04%)	0	(0.00%)	3	(0.07%)	5	(0.33%)	0	(0.00%)	9	(0.09%)

[1] Participants with unmarked ethnicity are classified as minority.
[2] Mean follow-up is the number of months from enrollment to the last Form 33 or date of death from Form 124 (Final Report of Death).
[3] Excludes one case with borderline malignancy.
[4] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.
[5] Only one report of "other cancer" or "other fracture" is reported; however, the first other cancer or other fracture of each type is adjudicated.
[6] "Other fracture" excludes fractures indicated as pathological.

Table 9.14
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Observational Study
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
No. of participants w/ Form 33	40684		6933		8673		16283		8795		5348		35336	
Mean follow-up (months) [2]	15.8		15.8		15.8		16.0		15.5		15.6		15.8	
Outcomes														
Cardiovascular														
MI	40	(0.07%)	3	(0.03%)	2	(0.02%)	16	(0.07%)	19	(0.17%)	1	(0.01%)	39	(0.08%)
Sudden coronary death	9	(0.02%)	0	(0.00%)	1	(0.01%)	2	(0.01%)	6	(0.05%)	1	(0.01%)	8	(0.02%)
Angina	110	(0.21%)	9	(0.10%)	9	(0.08%)	51	(0.23%)	41	(0.36%)	15	(0.22%)	95	(0.20%)
Congestive heart failure	51	(0.10%)	3	(0.03%)	4	(0.04%)	21	(0.10%)	23	(0.20%)	10	(0.14%)	41	(0.09%)
CABG/PTCA	74	(0.14%)	4	(0.04%)	4	(0.04%)	34	(0.16%)	32	(0.28%)	7	(0.10%)	67	(0.14%)
Carotid artery disease	22	(0.04%)	1	(0.01%)	1	(0.01%)	8	(0.04%)	12	(0.11%)	4	(0.06%)	18	(0.04%)
Stroke	49	(0.09%)	2	(0.02%)	6	(0.05%)	18	(0.08%)	23	(0.20%)	10	(0.14%)	39	(0.08%)
PVD	13	(0.02%)	1	(0.01%)	1	(0.01%)	5	(0.02%)	6	(0.05%)	0	(0.00%)	13	(0.03%)
DVT	4	(0.01%)	0	(0.00%)	0	(0.00%)	2	(0.01%)	2	(0.02%))	0	(0.00%	4	(0.01%)
PE	3	(0.01%)	0	(0.00%)	0	(0.00%)	0	(0.00%)	3	(0.03%)	0	(0.00%)	3	(0.01%)
Cancer														
Breast cancer [3]	112	(0.21%)	19	(0.21%)	15	(0.13%)	51	(0.23%)	27	(0.24%)	9	(0.13%)	103	(0.22%)
Invasive breast cancer [4]	91	(0.17%)	16	(0.18%)	12	(0.11%)	40	(0.18%)	23	(0.20%)	7	(0.10%)	84	(0.18%)
In situ breast cancer	22	(0.04%)	4	(0.04%)	3	(0.03%)	11	(0.05%)	4	(0.04%)	2	(0.03%)	20	(0.04%)
Ovary cancer	8	(0.01%)	1	(0.01%)	3	(0.03%)	4	(0.02%)	0	(0.00%)	0	(0.00%)	8	(0.02%)
Endometrial cancer [5]	19	(0.06%)	1	(0.02%)	2	(0.03%)	9	(0.07%)	7	(0.11%)	5	(0.14%)	14	(0.05%)
Colo-rectal cancer	26	(0.05%)	0	(0.00%)	3	(0.03%)	11	(0.05%)	12	(0.11%)	4	(0.06%)	22	(0.05%)
Other (non-skin) cancer [6]	80	(0.15%)	3	(0.03%)	11	(0.10%)	35	(0.16%)	31	(0.27%)	8	(0.12%)	72	(0.15%)

Table 9.14 (continued)
Counts (Annualized Percentages) of Participants with Locally Verified Outcomes for Observational Study
Data as of: 08/31/97

	Total		Age								Ethnicity			
			50-54		55-59		60-69		70-79		Minority[1]		White	
Fractures														
Hip fracture	16	(0.03%)	2	(0.02%)	1	(0.01%)	5	(0.02%)	8	(0.07%)	1	(0.01%)	15	(0.03%)
Vertebral fracture	21	(0.04%)	1	(0.01%)	3	(0.03%)	7	(0.03%)	10	(0.09%)	0	(0.00%)	21	(0.05%)
Other fracture [6,7]	229	(0.43%)	21	(0.23%)	44	(0.39%)	103	(0.47%)	61	(0.54%)	16	(0.23%)	213	(0.46%)
Other														
Deaths	39	(0.07%)	1	(0.01%)	4	(0.04%)	13	(0.06%)	21	(0.18%)	9	(0.13%)	30	(0.06%)

[1] Participants with unmarked ethnicity are classified as minority.
[2] Mean follow-up is the number of months from enrollment to the last Form 33 or date of death from Form 124 (Final Report of Death).
[3] Excludes two cases with borderline malignancy.
[4] Includes one case with unknown tumor behavior.
[5] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.
[6] Only one report of "other cancer" or "other fracture" is reported; however, the first other cancer or other fracture of each type is adjudicated.
[7] "Other fracture" excludes fractures indicated as pathological.

Table 9.15
Counts (Annualized Percentages) of HRT Participants With and Without Uterus
Data as of: 08/31/97

	With Uterus		Without Uterus		Z[1]
No. of participants w/ Form 33	9640		6278		
Mean follow-up (months) [2]	16.2		16.6		
Outcomes					
Cardiovascular					
CHD (MI or Sudden coronary death)	26	0.20%	16	0.18%	-0.47
MI	25	0.19%	14	0.16%	-0.75
Sudden coronary death	3	0.02%	3	0.03%	0.90
Angina	28	0.21%	28	0.32%	0.81
Congestive heart failure	10	0.08%	14	0.16%	0.71
CABG/PTCA	29	0.22%	18	0.21%	-0.47
Carotid artery disease	7	0.05%	4	0.05%	0.00
Stroke	9	0.07%	18	0.21%	1.64
PVD	1	0.01%	5	0.06%	1.55
DVT	18	0.14%	4	0.05%	-2.76
PE	9	0.07%	2	0.02%	-1.73
Cancer					
Breast cancer	16	0.12%	9	0.10%	-1.06
Invasive breast cancer	12	0.09%	6	0.07%	-0.62
In situ breast cancer	4	0.03%	3	0.03%	-0.32
Ovary cancer	1	0.01%	2	0.02%	1.16
Colo-rectal cancer	8	0.06%	8	0.09%	1.53
Other (non-skin) cancer [3]	29	0.22%	24	0.28%	0.55
Fractures					
Hip fracture	1	0.01%	4	0.05%	1.67
Vertebral fracture	9	0.07%	4	0.05%	-1.55
Other fracture [3]	130	1.00%	85	0.98%	-0.98
Other					
Deaths	12	0.09%	13	0.15%	0.50

1 Z-statistic computed using a stratified weighted log-rank test. Weights are linear between 0 and 3 years for cardiovascular outcomes and fractures, and linear between 0 and 10 years for cancer outcomes and death, and are constant thereafter. The tests are stratified on baseline agegroup (50-54, 55-59, 60-69, 70-79) and prevalent condition status. The no prevalent condition strata are further stratified on participating in DM and participating in CaD.
2 Mean follow-up is the number of months from enrollment to the last Form 33 or date of death from Form 124 (Final Report of Death).
3 Only one report or "other cancer" or "other fracture" is reported; however, the first other cancer or other fracture of each type is adjudicated.

10. Clinical Center Performance Monitoring

10.1 Performance Monitoring

A four step plan is used to identify clinic-specific performance issues in a timely fashion, to reinforce good performance, and to provide assistance or institute corrective action if performance is inadequate. The Performance Monitoring Committee (PMC) Report, updated quarterly, summaries clinic-specific performance (see *Table 10.1 - Clinical Center Performance Summary* for cumulative data through August 31, 1997).

10.2 PMC Committee Activity

Over the past six months, the PMC continued to monitor Clinical Center progress in recruitment closely. In addition to routine recruitment monitoring, the PMC:

- Approved requirements for CCs to document plans and procedures for screening and randomizing participants at remote sites, with review by the Project Office and CCC before implementation. Limiting the randomizations at remote sites will help prevent randomization of DM participants with limited access to DM Intervention groups and help ensure access of participants to clinic staff.

The PMC continued to focus more attention on adherence, retention and outcomes issues. PMC activities directed to adherence issues included:

- Conducting PMC visits focusing on adherence/retention issues.
- Recommending an HRT adherence/retention working group meeting, with attendees to include clinic Lead Practitioners and consulting gynecologists.
- Updating and distributing an updated randomization/follow-up plan to all CCs. The updated plan included all follow-up contacts, including routine clinic visits, phone contacts, and mail contacts and provides the CCs with a tool to estimate future CC workload.
- Working with the National CM Committee chair to provide updates to the Hot Tips (written suggestions) directed at CC management support
- Reviewing DM additional assistance data to determine effective strategies to enhance DM Intervention adherence.
- Reviewing and providing feedback to the SC on proposed CT/OS follow-up goals and guidelines.

Additional outcomes activities included:

- Adding a conference call or meeting with the clinic PI, physician adjudicator, and Outcomes Specialists before or during PMC visits.

- Reviewing and updating all PMC members on current outcomes reports included in the monthly activity reports distributed by the CCC.

- Reviewing summary outcomes data included in the summary of clinic performance for each clinic.

- Conducting outcomes-specific conference calls with CCs.

From March 1 through August 31, the PMC held one to two conference calls per month. During this period the PMC conducted five Level 4 visits to clinics and held six follow-up conference calls with CCs to follow the CCs progress on recommendations made at a previous PMC visit. The PMC also conducted six conference calls in place of visits for those CCs that would benefit from interaction with the PMC but for which a visit was not judged to be necessary and as follow-up with clinics after a PMC visit, including two outcomes-specific calls.

Specific plans for the next six months include developing a step-by-step adherence and retention template which Clinical Centers can use to optimize and enhance their adherence and retention efforts.

Table 10.1
CC Performance Summary

Summary - VCC

	Recruitment		HRT Follow-up		DM Follow-up		Retention		HRT Intervention		DM Intervention		CaD Intervention		Outcomes		Central Lab		Data	
	June - Aug. 97	cum., Aug 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97
Atlanta	77	66	92	91	89	87	7.4	7.7	75	73	11.4	11.1	63	63	28	29	94	94	95	95
Birmingham	73	73	92	91	91	88	7.5	7.2	83	80	7.1	6.9	62	61	24	24	96	96	80	79
Bowman	-	79	83	84	78	77	6.1	6.5	79	74	9.5	9.3	63	66	41	31	96	96	91	92
Brigham	75	63	94	94	89	87	6.3	6.3	84	80	11.2	11.3	70	66	32	29	95	95	70	71
Buffalo	-	94	84	83	82	83	6.6	7.0	78	74	10.2	10.1	65	67	54	58	95	95	97	97
Chicago	-	88	73	75	61	62	5.0	5.6	79	80	11.6	11.3	54	57	30	31	97	97	78	80
Iowa	-	94	95	95	95	95	2.6	2.8	90	89	12.3	12.4	76	75	33	39	97	97	93	93
LaJolla	87	74	82	83	79	82	9.1	9.2	75	71	9.6	10.5	69	66	35	48	95	95	91	91
Memphis	89	78	89	86	83	80	6.7	7.0	82	81	10.8	10.8	59	60	21	27	92	92	68	69
Minneapolis	104	80	94	93	89	87	4.3	4.6	84	81	12.7	12.6	71	67	47	43	99	99	92	93
Newark	150	83	81	80	73	72	3.6	4.3	79	78	10.9	11.4	51	51	41	35	96	96	82	83
Pawtucket	124	76	83	84	77	80	6.0	6.1	80	80	11.5	11.5	60	66	51	44	96	96	80	80
Pittsburgh	-	86	68	69	62	59	3.3	4.1	86	84	11.9	11.9	68	69	38	41	97	97	86	86
Seattle	-	97	71	75	72	74	4.7	5.5	81	79	14.0	13.4	62	66	36	40	93	94	75	76
Tucson	93	89	67	67	66	62	8.0	7.9	71	61	10.0	9.8	53	49	48	50	91	91	91	91
UCDavis	-	107	81	84	82	82	4.6	5.1	83	79	9.8	9.9	65	63	32	39	96	96	75	74

Note: Summary data is taken from the summary columns of the following reports.

Table 10.1
CC Performance Summary

Summary - NCC

	Recruitment		HRT Followup		DM Followup		Retention		HRT Intervention		DM Intervention		CaD Intervention		Outcomes		Central Labs		Data	
	June - Aug. 97	cum., Aug 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97
Chapel Hill	78	72	90	92	83	82	1.4	2.0	89	87	9.5	9.6	64	58	61	50	95	95	76	78
Chi-Rush	188	121	84	88	81	88	1.7	1.9	63	72	9.0	8.2	53	60	59	44	91	92	67	72
Cincinnati	72	60	93	89	85	81	2.3	2.6	87	88	11.6	10.8	63	65	31	23	92	92	74	75
Columbus	143	80	90	92	68	76	3.2	3.2	86	85	13.3	11.6	65	70	52	62	92	94	85	86
Detroit	93	63	68	66	69	60	1.9	2.6	79	73	10.6	12.2	56	56	27	35	92	92	82	82
Gainesville	93	87	91	90	89	88	4.3	4.6	90	88	12.5	11.1	64	69	55	67	92	91	96	96
GWU-DC	81	79	94	92	90	89	3.3	3.9	88	80	11.9	12.1	68	64	43	39	95	95	97	97
Honolulu	74	62	87	88	83	87	2.1	2.3	87	89	11.2	11.0	63	70	61	57	97	98	87	88
Houston	59	59	88	82	67	66	2.4	2.6	91	83	10.5	10.0	74	73	26	27	90	90	85	86
Irvine	100	78	50	61	52	59	4.6	4.7	80	79	11.2	9.5	4	32	15	47	96	97	58	61
LA	111	78	86	88	81	76	5.4	4.7	87	81	11.9	9.6	62	59	43	47	97	97	78	80
Madison	84	85	96	95	94	94	3.2	3.7	89	86	13.3	14.3	74	72	82	79	98	98	98	98
Mediantic	82	55	82	81	75	73	5.0	3.9	76	73	7.9	6.1	59	51	21	11	90	89	87	87
Miami	102	65	67	69	38	46	2.3	2.8	83	75	8.0	8.3	62	56	24	38	96	96	86	86
Milwaukee	104	84	95	96	93	95	2.2	2.8	90	89	12.7	11.4	81	80	44	27	96	96	94	93
Nevada	100	88	88	87	89	87	3.3	3.5	86	84	15.4	17.6	68	70	39	42	96	97	97	97
NY City	92	69	91	90	89	88	3.7	5.0	82	77	9.2	10.2	64	57	38	32	89	90	87	87
Oakland	96	77	89	90	86	85	2.0	2.0	93	87	13.9	13.0	75	79	28	28	94	95	82	83
Portland	82	70	85	84	83	84	2.3	2.6	90	81	11.6	12.3	73	67	27	23	94	94	58	61
San Antonio	101	71	67	67	48	52	3.2	3.9	86	84	12.3	9.2	59	64	57	53	93	93	93	93
Stanford	90	84	89	92	87	92	1.6	1.9	88	86	13.2	12.0	73	78	58	50	96	96	87	87
Stony Brook	63	64	98	99	98	98	3.1	3.5	92	88	11.1	12.7	66	67	77	72	95	95	98	98
Torrance	102	83	84	82	80	79	2.9	3.3	88	80	13.6	14.1	70	65	70	35	96	96	81	82
Worcester	111	74	91	90	83	85	3.2	3.4	90	89	12.5	12.1	69	62	17	44	91	93	87	85

Note: Summary data is taken from the summary columns of the following reports.

Table 10.1 (continued)

Recruitment - VCC

	HRT[1] % goal			DM[1] % goal			CaD[2] % goal			OS[3] % goal			Age - HRT[4] % goal, 70 - 79			Age - DM[4] % goal, 70 - 79			Overall weighted average*		
	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97
Atlanta	66	72	66	141	80	101	78	85	50	16	41	75	84	72	37	113	92	52	91	77	66
Birmingham	112	117	88	146	50	96	29	34	48	111	69	113	64	147	51	117	39	45	95	73	73
Bowman	-	-	101	-	-	102	64	73	42	191	156	100	-	-	75	-	-	54	-	-	79
Brigham	103	149	69	51	43	93	51	58	45	50	44	70	77	91	41	21	25	45	63	75	63
Buffalo	-	-	112	-	-	108	58	75	63	122	16	101	-	-	113	-	-	69	-	-	94
Chicago	-	-	93	-	-	115	29	35	45	122	239	85	-	-	102	-	-	99	-	-	88
Iowa	175	184	128	-	-	95	58	68	60	182	139	139	130	202	106	-	-	60	-	-	94
LaJolla	95	84	75	150	145	95	69	47	52	101	65	102	77	70	67	92	84	71	100	87	74
Memphis	85	92	90	69	57	88	64	47	58	64	92	100	128	211	80	100	111	58	82	89	78
Minneapolis	151	165	98	64	107	97	50	48	51	66	66	117	156	128	77	72	83	54	93	104	80
Newark	221	196	88	167	141	109	50	86	53	70	61	131	254	283	75	177	114	65	158	150	83
Pawtucket	159	147	82	158	113	99	61	75	55	33	18	97	130	221	64	124	158	63	121	124	76
Pittsburgh	-	-	108	-	-	111	60	86	47	15	17	86	-	-	90	-	-	63	-	-	86
Seattle	-	-	119	-	-	108	75	66	48	43	6	75	-	-	134	-	-	100	-	-	97
Tucson	117	156	78	59	50	104	49	67	48	61	40	138	291	166	110	112	56	120	104	93	89
UCDavis	-	-	111	-	-	132	65	94	59	102	176	101	-	-	126	-	-	127	-	-	107
*weights:		1			1			1			0.25			0.5			0.5				

[1] From WHIP1109. Distributed in CC Monthly Activity Reports. Can be run at CC as WHIP0770.
[2] From WHIP1125. Distributed in CC Monthly Activity Reports. Can be run at CC as WHIP1139.
[3] From WHIP1126. Distributed in CC Monthly Activity Reports. Can be run at CC as WHIP1139.
[4] Derived from WHIP0578. Available at CC as WHIP0775.

Table 10.1 (continued)

Recruitment - NCC

	HRT[1] % goal			DM[1] % goal			CaD[2] % goal			OS[3] % goal			Age - HRT[4] % goal, 70 - 79			Age - DM[4] % goal, 70 - 79			Overall weighted average*		
	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97	Mar. - May	June - Aug.	cum. Aug. 97
Chapel Hill	144	110	73	138	93	102	63	66	51	113	101	123	144	58	54	50	17	40	111	78	72
Chi-Rush	270	202	167	270	204	150	68	156	60	391	355	190	58	173	103	99	124	78	185	188	121
Cincinnati	83	89	58	69	88	68	50	45	63	133	112	106	57	62	45	44	50	38	67	72	60
Columbus	122	142	75	150	193	109	70	71	63	111	102	114	130	173	64	116	182	64	116	143	80
Detroit	130	121	76	154	170	77	40	31	65	91	122	93	50	43	35	37	45	20	92	93	63
Gainesville	133	94	121	107	113	91	50	73	54	74	71	136	124	103	85	86	95	55	97	93	87
GWU-DC	124	86	86	138	107	99	49	65	53	72	27	158	108	86	74	33	70	42	94	81	79
Honolulu	61	70	55	104	97	93	60	70	44	92	94	121	29	58	42	41	45	39	67	74	62
Houston	77	86	68	114	95	83	31	36	48	25	32	96	22	22	25	17	25	31	58	59	59
Irvine	117	92	79	105	79	88	75	136	54	153	38	179	151	137	80	78	83	47	106	100	78
LA	95	121	77	152	109	96	55	81	57	75	81	95	166	202	85	239	83	72	123	111	78
Madison	146	67	104	130	107	91	104	97	66	36	114	129	158	58	86	74	58	52	119	84	85
Medlantic	32	88	59	41	164	76	35	43	43	81	18	91	7	50	37	8	45	28	32	82	55
Miami	151	104	88	146	139	84	52	81	50	91	168	83	58	43	30	70	87	39	103	102	65
Milwaukee	140	121	107	99	88	95	82	98	58	63	107	102	223	144	88	107	74	52	118	104	84
Nevada	158	119	104	154	135	93	76	79	59	72	75	133	216	79	100	182	70	68	142	100	88
NY City	100	96	72	81	121	76	38	33	54	72	102	130	109	109	69	59	127	48	75	92	69
Oakland	113	115	89	80	98	96	52	53	44	85	110	145	101	137	72	41	91	52	79	96	77
Portland	149	106	79	115	91	95	68	65	52	132	117	104	115	65	49	70	54	45	108	82	70
San Antonio	157	151	113	75	104	77	49	101	62	64	71	71	65	79	40	33	29	23	81	101	71
Stanford	93	78	82	110	110	88	81	83	66	104	93	125	160	103	101	139	77	79	108	90	84
Stony Brook	72	41	66	92	73	73	31	68	54	46	63	96	108	65	63	83	74	47	71	63	64
Torrance	108	86	74	144	128	110	48	82	59	145	114	130	125	106	66	171	116	92	114	102	83
Worcester	90	121	63	84	137	93	91	65	63	46	62	132	130	151	64	103	116	63	92	111	74
*weights:		1			1			1			0.25			0.5			0.5				

[1] From WHIP1109. Distributed in CC Monthly Activity Reports. Can be run at CC as WHIP0770.
[2] From WHIP1125. Distributed in CC Monthly Activity Reports. Can be run at CC as WHIP1139.
[3] From WHIP1126. Distributed in CC Monthly Activity Reports. Can be run at CC as WHIP1139.
[4] Derived from WHIP0578. Available at CC as WHIP0775.

Table 10.1 (continued)

Minority Randomization/Enrollment at Pool 1 Clinics

	% Non-white HRT/DM/OS[1]		
VCCs	cum., May 97	cum., Aug. 97	
Atlanta	29	28	
Birmingham	42	41	
LaJolla	26	27	
Tucson	22	23	
NCCs			
Chi-Rush	55	56	
Detroit	30	31	
Honolulu	73	73	
Medlantic	65	63	
Miami	44	44	
San Antonio	41	45	

[1] Derived from WHIP0960. Can be run at CC as WHIP777.

Table 10.1 (continued)

HRT Follow-up - VCC

	6 Week[1]		Semi-Annual 1[2]				Annual Visit 1[2]				Semi-Annual 2[2]				Annual Visit 2[2]				Semi-Annual 3[2]				Annual Visit 3[2]				Semi-Annual Visit 4[2]				Overall		
	Conducted		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks				
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Atlanta	95	95	99	99	92	91	98	99	96	96	94	94	81	81	93	93	90	90	93	89	81	80		89		89					92	91	
Birmingham	92	93	97	97	86	86	98	98	85	85	98	98	87	86	98	98	90	89	97	97	88	88	97	97	89	87		80		80	92	91	
Bowman	95	95	97	97	85	85	94	95	70	74	88	89	60	67	93	93	73	73	86	88	64	71	92	92	81	78					83	84	
Brigham	97	97	99	99	93	94	99	99	94	94	97	98	92	92	96	97	91	91	90	94	89	90	92	91	89	88					94	94	
Buffalo	97	97	97	97	84	85	94	95	82	82	90	90	73	72	93	95	78	79	83	92	67	70	87	81	73	63		80		70	84	83	
Chicago	89	90	95	95	66	66	93	94	54	53	90	92	59	62	89	91	44	47	82	83	62	61	70	76	60	63					73	75	
Iowa	100	100	99	99	94	94	99	99	93	92	99	99	93	92	97	98	89	89	97	97	90	89	98	98	93	90					95	95	
LaJolla	89	90	93	93	75	77	89	89	72	73	85	87	71	74	87	88	73	72	86	88	72	77	86	90	86	87					82	83	
Memphis	90	91	98	98	85	84	97	97	90	89	92	92	75	75	96	96	85	85	93	92	79	78	92	95	88	88		76		57	89	86	
Minneapolis	100	100	100	100	90	91	100	100	92	92	98	98	87	88	98	98	86	89	97	96	86	84	97	97	87	88		95		80	94	93	
Newark	91	91	95	96	69	73	97	95	74	74	89	89	56	56	92	92	75	71	90	90	61	61	93	95	70	59					81	80	
Pawtucket	96	96	96	96	81	83	95	96	55	60	92	92	67	70	94	94	77	78	91	91	76	77	85	89	76	76					83	84	
Pittsburgh	91	95	99	94	64	56	96	95	42	43	95	95	58	59	94	94	12	19	94	94	43	47	69	82	33	24					68	69	
Seattle	95	96	96	96	58	60	93	95	60	63	89	92	36	47	85	91	40	46	85	87	41	49	85	89	61	59					71	75	
Tucson	82	82	93	92	60	60	91	90	65	65	87	86	52	49	85	86	31	34	74	80	42	38	75	75	38	34					67	67	
UCDavis	94	95	98	98	83	84	95	95	69	73	94	93	83	83	91	94	69	74	86	89	74	77	79	80	43	61		79		79	81	84	

NOTES: Conducted = % of visits due for which at least one task has been key-entered.
+/- 2 weeks = % of visits due that have been conducted within 2 weeks of the target date.

[1] From WHIP1131. Can be run at CC as WHIP0781 or WHIP0786.
[2] From WHIP1141.

Table 10.1 (continued)

HRT Follow-up - NCC

	6 Week[1] Conducted		Semi-Annual 1[2] Conducted		Semi-Annual 1[2] +/- 2 wks		Annual Visit 1[2] Conducted		Annual Visit 1[2] +/- 2 wks		Semi-Annual 2[2] Conducted		Semi-Annual 2[2] +/- 2 wks		Annual Visit 2[2] Conducted		Annual Visit 2[2] +/- 2 wks		Overall		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Chapel Hill	97	96	99	99	79	81	100	99	67	78	100	98	88	86		100		87	90	92	
Chi-Rush	92	95	93	98	74	80	91	93	82	85	85	92	70	71					84	88	
Cincinnati	96	97	98	99	88	88	97	93	87	81	96	96	87	89		88		67	93	89	
Columbus	98	97	98	98	82	86	100	99	85	87	95	96	75	83					90	92	
Detroit	77	75	92	94	74	72	90	89	21	30	71	77	49	44		62		54	68	66	
Gainesville	99	99	98	99	88	88	95	95	77	80	94	95	77	80	96	93	92	80	91	90	
GWU-DC	98	97	100	99	93	92	99	98	92	91	93	96	85	86		88		77	94	92	
Honolulu	89	94	96	97	92	90	93	94	82	83	82	86	74	75		86		86	87	88	
Houston	98	98	95	95	81	82	94	91	80	78	80	81	61	61	100	81	100	70	88	82	
Irvine	74	76	88	92	50	59	66	79	24	35	44	61	3	22		73		55	50	61	
LA	99	100	99	99	84	86	94	96	75	79	83	90	64	71		94		81	86	88	
Madison	100	100	100	100	94	94	99	99	84	85	100	99	94	95		93		89	96	95	
Mediantic	98	99	98	97	70	70	95	93	71	72	84	82	56	54		89		72	82	81	
Miami	81	81	82	90	56	63	80	82	55	57	65	69	51	51		69		56	67	69	
Milwaukee	97	99	99	99	93	94	99	99	94	94	99	98	83	86		100		96	95	96	
Nevada	96	97	98	99	81	84	94	96	80	82	93	93	77	78		90		66	88	87	
NY City	96	97	98	98	92	92	97	97	84	86	92	93	78	81		83		83	91	90	
Oakland	96	97	98	99	87	88	97	97	78	84	95	94	76	79		94		82	89	90	
Portland	97	97	98	98	75	79	95	96	80	79	85	90	64	70		84		63	85	84	
San Antonio	65	69	83	84	66	66	79	81	60	62	71	67	42	40		74		60	67	67	
Stanford	90	95	99	99	85	86	97	96	92	90	94	97	67	79					89	92	
Stony Brook	100	100	100	100	98	98	99	99	95	96	100	100	97	99		100		100	98	99	
Torrance	90	91	93	92	75	75	94	94	78	83	88	86	70	68		76		76	84	82	
Worcester	97	98	99	99	83	84	96	98	87	88	98	92	78	74					91	90	

NOTES: Conducted = % of visits due for which at least one task has been key-entered.
+/- 2 weeks = % of visits due that have been conducted within 2 weeks of the target date.

[1] From WHIP1131. Can be run at CC as WHIP0781 or WHIP0786.
[2] From WHIP1141.

Table 10.1 (continued)

DM Follow-up - VCC

	Semi-Annual 1[1]				Annual Visit 1[1]				Semi-Annual 2[1]				Annual Visit 2[1]				Semi-Annual 3[1]				Annual Visit 3[1]				Semi-Annual Visit 4[1]				Overall	
	Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks			
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Atlanta	95	95	77	77	97	97	93	93	93	93	79	78	93	93	86	85	92	88	77	73	97	91	95	84					89	87	
Birmingham	99	99	85	86	99	98	87	86	97	98	84	85	97	97	87	87	95	96	83	83	96	93	90	87		79		57	91	88	
Bowman	87	88	63	64	91	92	75	77	82	83	61	63	90	90	70	72	80	81	59	60	91	88	82	78		77		62	78	77	
Brigham	99	99	80	79	98	98	91	91	95	96	72	73	96	96	86	86	96	95	73	73	94	96	88	88		76		67	89	87	
Buffalo	97	97	75	75	95	96	81	80	93	93	79	78	93	94	74	73	87	92	71	71	83	85	63	63		87		71	82	83	
Chicago	95	95	48	49	90	85	41	39	91	91	46	47	80	78	31	32	84	85	44	47	54	63	32	38					61	62	
Iowa	99	99	93	93	99	99	93	93	99	99	93	93	99	99	91	91	98	97	88	86	98	98	95	92					95	95	
LaJolla	91	91	58	61	90	91	77	79	85	87	60	64	86	87	72	73	85	85	67	70	89	88	85	82		94		94	79	82	
Memphis	94	94	72	72	96	96	83	83	89	89	65	64	93	94	82	83	89	88	58	60	91	92	86	85		71		55	83	80	
Minneapolis	99	99	78	78	99	99	90	90	96	97	78	78	98	99	87	88	94	95	66	65	96	97	89	90		84		64	89	87	
Newark	90	91	55	57	91	90	66	66	81	84	52	52	88	86	66	61	79	80	54	54	86	80	67	58					73	72	
Pawtucket	94	95	64	70	94	94	50	56	77	80	51	56	94	94	76	77	93	92	73	74	86	90	78	78					77	80	
Pittsburgh	98	97	57	55	95	96	37	39	86	86	40	39	93	96	12	22	84	86	29	27	80	84	38	25		37		37	62	59	
Seattle	96	96	50	50	95	96	56	59	92	92	51	51	93	95	48	50	90	92	47	50	89	93	61	62					72	74	
Tucson	96	96	66	66	94	94	67	68	90	91	51	49	88	89	30	37	78	86	28	27	83	83	25	38		43		7	66	62	
UCDavis	95	96	84	85	95	95	75	77	91	92	79	80	94	95	72	75	86	88	70	74	83	89	60	75		66		62	82	82	

NOTES: Conducted = % of visits due for which at least one task has been key-entered.
+/- 2 weeks = % of visits due that have been conducted within

[1] From WHIP1140.

Table 10.1 (continued)

DM Follow-up - NCC

	Semi-Annual 1[1]				Annual Visit 1[1]				Semi-Annual 2[1]				Annual Visit 2[1]				Overall		
	Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks		Conducted		+/- 2 wks				
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Chapel Hill	93	94	70	69	98	97	76	79	88	85	74	65		91		78	83	82	
Chi-Rush	93	96	74	79	87	90	69	72	91	95	75	75		100		100	81	88	
Cincinnati	94	95	81	82	95	92	87	79	90	91	74	74	89	79	72	59	85	81	
Columbus	92	93	56	55	93	96	68	69	56	68	43	51		93		83	68	76	
Detroit	93	85	73	68	79	78	21	30	78	77	69	62		42		36	69	60	
Gainesville	99	99	86	86	97	96	78	80	94	95	73	76	97	95	87	79	89	88	
GWU-DC	99	99	86	83	97	98	88	88	93	93	81	75	90	90	88	84	90	89	
Honolulu	98	97	80	79	93	92	86	84	97	95	74	79	76	95	57	77	83	87	
Houston	86	88	52	50	86	80	64	59	75	74	57	55	64	68	56	50	67	66	
Irvine	88	90	36	42	76	86	44	42	52	60	16	24		87		37	52	59	
LA	93	95	73	72	93	92	75	76	83	73	66	58		81		60	81	76	
Madison	100	100	94	94	97	98	88	88	98	98	90	90		96		88	94	94	
Medlantic	98	96	62	60	89	91	54	57	91	88	60	60	76	75	71	53	75	73	
Miami	67	86	51	47	50	66	24	39	20	23	14	16		53		38	38	46	
Milwaukee	100	100	90	90	100	99	92	92	99	99	80	84		98		95	93	95	
Nevada	99	99	84	82	96	98	84	85	95	96	74	72		95		70	89	87	
NY City	99	99	81	84	97	97	83	85	92	93	81	82		83		82	89	88	
Oakland	94	93	68	68	95	97	80	79	91	91	65	69	100	95	92	86	86	85	
Portland	95	96	82	82	94	95	65	68	88	89	74	76		92		75	83	84	
San Antonio	81	81	43	41	63	75	36	37	59	53	32	28	41	62	30	37	48	52	
Stanford	95	99	75	83	97	97	93	92	89	91	76	82		96		96	87	92	
Stony Brook	99	100	99	99	98	98	94	94	100	99	97	97		100		100	98	98	
Torrance	92	91	71	72	92	90	72	72	87	89	67	65		79		71	80	79	
Worcester	95	96	68	71	95	96	86	87	93	92	73	76	85	90	69	69	83	85	

NOTES: Conducted = % of visits due for which at least one task has been key-entered.
+/- 2 weeks = % of visits due that have been conducted within 2 weeks of the target date.

[1] From WHIP1140.

Table 10.1 (continued)

Retention - VCC

	HRT[1]				DM[2]				CaD[3]				OS			
	% Stopping Intervention		% Stopping Followup		% Stopping Intervention		% Stopping Followup		% Stopping Intervention		% Stopping Followup		% Stopping Followup		Overall	
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97
Atlanta	20.6	20.6	2.0	2.1	1.7	1.8	1.4	1.6	17.6	18.7	0.8	1.1	-	-	7.4	7.7
Birmingham	20.3	18.8	2.0	2.1	3.6	3.9	1.6	1.8	16.3	15.4	1.0	1.1	-	-	7.5	7.2
Bowman	14.9	18.3	2.4	1.9	2.3	2.5	2.5	2.3	14.0	14.0	0.3	0.0	-	-	6.1	6.5
Brigham	14.0	13.5	1.5	1.6	2.3	2.2	0.7	0.8	19.1	19.2	0.2	0.2	-	-	6.3	6.3
Buffalo	18.2	19.8	0.9	0.9	5.2	5.2	1.5	1.5	13.5	14.3	0.0	0.1	-	-	6.6	7.0
Chicago	11.5	13.0	0.6	0.5	1.7	1.6	1.5	1.6	12.2	14.7	2.4	2.4	-	-	5.0	5.6
Iowa	5.7	6.8	0.2	0.4	0.8	0.8	0.7	0.7	7.9	8.0	0.3	0.2	-	-	2.6	2.8
LaJolla	22.8	22.0	4.6	4.4	9.4	9.9	4.1	4.2	13.0	13.7	0.9	1.0	-	-	9.1	9.2
Memphis	13.3	14.2	1.4	1.5	2.7	2.6	1.5	1.5	21.2	21.8	0.2	0.3	-	-	6.7	7.0
Minneapolis	10.2	10.9	0.2	0.1	3.0	2.4	0.7	0.8	11.7	13.1	0.2	0.3	-	-	4.3	4.6
Newark	7.7	8.4	0.6	1.2	0.9	1.1	0.3	0.6	11.8	14.0	0.2	0.3	-	-	3.6	4.3
Pawtucket	14.7	14.2	1.9	1.9	3.0	2.7	1.2	1.2	14.5	16.0	0.8	0.7	-	-	6.0	6.1
Pittsburgh	9.9	11.2	1.1	1.4	0.4	1.1	0.4	0.9	7.8	9.5	0.0	0.2	-	-	3.3	4.1
Seattle	14.5	17.2	1.5	1.6	1.1	1.1	1.2	1.4	10.1	11.8	0.0	0.0	-	-	4.7	5.5
Tucson	19.1	19.6	3.7	3.7	2.4	2.4	1.7	1.7	20.3	19.1	0.7	0.8	-	-	8.0	7.9
UCDavis	10.7	12.2	2.0	2.1	2.9	3.2	1.6	1.8	9.9	10.7	0.6	0.6	-	-	4.6	5.1

[1] From report WHIP0745.
[2] From report WHIP0748.
[3] From report WHIP0744.

Table 10.1 (continued)

Retention - NCC

	HRT[1]				DM[2]				CaD[3]				OS			
	% Stopping Intervention		% Stopping Followup		% Stopping Intervention		% Stopping Followup		% Stopping Intervention		% Stopping Followup		% Stopping Followup		Overall	
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97
Chapel Hill	3.1	5.0	0.0	0.5	0.3	0.3	0.5	0.4	4.2	5.5	0.0	0.4	-	-	1.4	2.0
Chi-Rush	5.3	6.7	0.8	0.7	0.4	0.7	0.5	0.7	1.5	2.8	1.5	0.0	-	-	1.7	1.9
Cincinnati	5.4	6.0	0.3	0.3	0.0	0.0	0.0	0.0	8.0	9.1	0.0	0.0	-	-	2.3	2.6
Columbus	6.8	7.2	0.6	0.8	0.6	0.8	0.3	0.4	10.8	10.0	0.0	0.0	-	-	3.2	3.2
Detroit	2.7	4.0	0.6	1.3	2.8	2.2	1.3	1.6	3.3	6.1	0.7	0.6	-	-	1.9	2.6
Gainesville	8.9	10.9	0.7	1.0	1.2	2.0	0.2	0.3	14.2	12.9	0.7	0.3	-	-	4.3	4.6
GWU-DC	9.8	12.2	0.5	0.7	3.1	2.8	0.9	1.2	4.8	6.4	0.4	0.3	-	-	3.3	3.9
Honolulu	6.6	7.1	1.2	1.1	0.3	0.3	0.0	0.0	4.5	5.0	0.0	0.0	-	-	2.1	2.3
Houston	9.9	9.0	0.3	0.3	0.0	0.0	0.0	0.0	3.9	6.0	0.0	0.0	-	-	2.4	2.6
Irvine	11.9	15.3	1.4	1.2	0.0	0.0	1.4	1.5	6.3	6.3	6.3	4.0	-	-	4.6	4.7
LA	6.0	5.8	0.9	1.0	1.6	1.4	0.9	0.8	21.6	18.2	1.1	0.8	-	-	5.4	4.7
Madison	7.6	9.4	0.4	0.6	0.3	1.5	0.6	0.7	10.0	10.1	0.0	0.0	-	-	3.2	3.7
Medlantic	10.5	8.5	2.3	1.6	6.1	4.7	2.1	1.6	7.1	6.2	1.9	1.0	-	-	5.0	3.9
Miami	4.8	7.0	0.8	1.5	2.8	2.9	0.2	0.5	3.0	4.0	2.0	1.1	-	-	2.3	2.8
Milwaukee	6.1	8.6	0.4	0.4	0.3	0.6	0.0	0.1	6.1	7.0	0.0	0.0	-	-	2.2	2.8
Nevada	6.6	7.9	0.6	0.6	1.8	1.2	0.8	0.7	9.8	10.8	0.0	0.0	-	-	3.3	3.5
NY City	9.8	11.5	1.3	1.7	1.5	1.8	0.9	1.2	8.7	13.3	0.0	0.4	-	-	3.7	5.0
Oakland	3.5	4.3	0.5	0.4	1.0	1.1	1.0	1.2	6.2	5.1	0.0	0.0	-	-	2.0	2.0
Portland	4.2	5.0	0.8	1.0	0.3	0.6	0.5	0.7	7.7	7.8	0.0	0.7	-	-	2.3	2.6
San Antonio	7.0	7.5	1.4	1.7	0.8	1.4	1.0	1.7	8.5	8.6	0.6	2.6	-	-	3.2	3.9
Stanford	5.0	6.3	0.0	0.0	0.6	0.5	0.6	0.5	3.1	4.0	0.4	0.3	-	-	1.6	1.9
Stony Brook	6.9	8.8	0.0	0.0	0.8	0.8	0.0	0.0	11.0	11.1	0.0	0.0	-	-	3.1	3.5
Torrance	6.7	9.0	0.8	0.7	1.5	1.7	0.6	0.5	7.9	7.7	0.0	0.0	-	-	2.9	3.3
Worcester	10.0	8.9	0.8	0.6	1.1	1.5	0.6	0.6	6.7	8.6	0.0	0.0	-	-	3.2	3.4

[1] From report WHIP0745.
[2] From report WHIP0748.
[3] From report WHIP0744.

Table 10.1 (continued)

HRT Intervention - VCC

	% with Pill Count at AV1[1]		% ≥ 80% Adherent at AV1[2]		Adherence Summary at AV1[3]		% with Pill Count at AV2[1]		% ≥ 80% Adherent at AV2[2]		Adherence Summary at AV2[3]		% with Pill Count at AV3[1]		% ≥ 80% Adherent at AV3[2]		Adherence Summary at AV3[3]		% Blinding[4]		Overall Weighted ave*		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Atlanta	89	89	79	80	68	69	75	74	79	77	54	53		67		86		49	91	91	75	73	
Birmingham	90	90	86	86	77	76	81	81	87	86	71	71		76		83		65	93	93	83	80	
Bowman	87	88	80	79	67	67	79	80	89	90	65	65		72		73		44	94	92	79	74	
Brigham	91	92	89	89	81	81	85	82	83	85	69	68		71		88		59	94	93	84	80	
Buffalo	88	87	84	85	71	71	73	75	85	83	59	60		75		74		46	88	88	78	74	
Chicago	88	90	84	84	68	71	81	82	83	83	61	63		86		96		62	93	93	79	80	
Iowa	96	96	92	92	87	87	91	91	92	93	83	85		82		95		79	92	92	90	89	
LaJolla	89	89	81	81	62	62	80	80	78	80	52	54		64		80		44	92	92	75	71	
Memphis	91	91	84	84	75	75	84	83	84	84	69	68		81		88		69	93	93	82	81	
Minneapolis	93	92	86	86	80	79	84	85	86	86	70	72		82		81		64	94	94	84	81	
Newark	91	92	78	79	68	68	86	86	80	78	62	60		79		84		68	93	93	79	78	
Pawtucket	89	89	85	87	71	74	78	79	87	88	64	65		73		93		64	93	93	80	80	
Pittsburgh	93	94	89	89	79	80	85	86	89	90	73	75		80		91		60	98	98	86	84	
Seattle	91	91	87	88	74	77	81	81	86	83	58	61		71		93		59	95	94	81	79	
Tucson	79	80	80	79	58	57	74	72	74	72	47	44		61		44		22	94	95	71	61	
UCDavis	90	91	89	88	77	77	85	84	88	86	68	68		74		83		51	91	90	83	79	
*Weights	1		1		1		1		1		1		1		1		1		0.5				

[1] % of AVs conducted that include study pill collections or estimates. From WHIP1141.

[2] % of ppts adherent as measured by pill count or estimate at AVs, excluding ERT→PERT participants. From data analysis not yet routinely distributed to CCs.

[3] % of ppts due for the AV who took at least 80% of their study pills.

[4] % of ppts for whom no unblinding occurred. From DSMB report not distributed to CCs.

Table 10.1 (continued)

HRT Intervention - NCC

	% with Pill Count at AV1[1]		% ≥ 80% Adherent at AV1[2]		Adherence Summary at AV1[3]		% with Pill Count at AV2[1]		% ≥ 80% Adherent at AV2[2]		Adherence Summary at AV2[3]		% with Pill Count at AV3[1]		% ≥ 80% Adherent at AV3[2]		Adherence Summary at AV3[3]		% Blinding[4]		Overall Weighted ave*		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Chapel Hill	95	97	87	89	82	84		93		79		73							96	94	89	87	
Chi-Rush	80	85	52	66	38	53													99	98	63	72	
Cincinnati	89	89	89	89	77	74		90		100		79							96	95	87	88	
Columbus	91	90	85	83	76	74													97	97	86	85	
Detroit	89	90	78	78	62	62		75		83		42							96	94	79	73	
Gainesville	95	94	94	91	84	81	83	90	100	93	79	78							96	96	90	88	
GWU-DC	92	92	89	87	80	79		71		90		56							93	90	88	80	
Honolulu	96	95	86	87	77	78		92		100		79							89	89	87	89	
Houston	94	94	94	93	83	79	92	83	92	86	85	58							97	97	91	83	
Irvine	89	88	90	86	52	60		75		100		55							97	97	80	79	
LA	93	93	87	88	77	76		73		91		63							92	92	87	81	
Madison	94	94	89	90	82	83		84		91		73							93	92	89	86	
Mediantic	86	88	72	73	58	60		76		75		51							97	97	76	73	
Miami	92	90	87	83	62	61		82		78		44							98	98	83	75	
Milwaukee	95	96	90	90	85	86		89		92		82							93	91	90	89	
Nevada	93	91	86	87	75	76		85		91		71							96	94	86	84	
NY City	90	91	80	81	69	71		70		86		52							95	94	82	77	
Oakland	98	98	93	90	86	86		100		75		71							94	92	93	87	
Portland	93	94	92	90	81	81		69		91		53							97	96	90	81	
San Antonio	93	95	92	92	67	69		86		94		60							97	97	86	84	
Stanford	91	91	90	89	79	78													92	90	88	86	
Stony Brook	96	94	92	87	87	80		95		89		84							93	90	92	88	
Torrance	89	92	94	88	78	76		75		92		52							94	93	88	80	
Worcester	94	89	92	92	82	81													96	95	90	89	
*Weights	1		1		1		1		1		1		1		1		1		0.5				

[1] % of AVs conducted that include study pill collections or estimates. From WHIP1141.

[2] % of ppts adherent as measured by pill count or estimate at AVs, excluding ERT→ PERT participants. From data analysis not yet routinely distributed to CCs.

[3] % of ppts due for the AV who took at least 80% of their study pills.

[4] % of ppts for whom no unblinding occurred. From DSMB report not distributed to CCs.

Table 10.1 (continued)

VCC- DM Intervention - Participation, Adherence, and Retention[1]

	Session Participation						Fat Gram Scores Session 12						% Stop Inter % Stop FU[8]		AV1 w/o Inter[9]		[Cont-Inter]%fat AV1[10]			
	% Attendance Session 12[2]		% Completion Session 12[3]		% Missed 3 Consecutive Sessions[4]		% Collected[5]		% < goal[6]		(% < goal) * (% collected)[7]		FU	Interv			FFQ	4DFR		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., Aug. 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., Aug. 97	cum., Aug. 97	Weighted Value	
Atlanta	70	69	89	90	14.8	15.6	84	84	72	72	60	60	1.6	1.8	1.4	1.2	10.4	13.1	11.1	
Birmingham	63	64	90	90	12.2	13.6	85	85	69	67	59	57	1.8	3.9	5.6	6.7	7.1	6.3	6.9	
Bowman	74	70	85	86	17.2	18.8	78	72	68	68	53	49	2.3	2.5	7.2	6.6	10.2	6.7	9.3	
Brigham	74	74	94	95	7.6	8.4	89	90	73	73	65	66	0.8	2.2	2.9	3.8	10.6	13.3	11.3	
Buffalo	75	74	95	94	1.2	2.6	82	82	59	59	48	48	1.5	5.2	2.4	2.2	10.4	9.0	10.1	
Chicago	78	79	90	90	7.0	7.3	91	91	72	73	66	66	1.6	1.6	5.1	4.6	11.1	11.9	11.3	
Iowa	74	74	99	99	0.3	0.3	96	96	80	80	77	77	0.7	0.8	3.5	3.2	12.8	11.2	12.4	
LaJolla	70	70	86	85	11.3	13.0	75	74	72	68	54	50	4.2	9.9	7.7	7.2	9.7	12.9	10.5	
Memphis	74	72	87	92	13.6	16.2	80	86	76	74	61	64	1.5	2.6	2.1	2.3	10.8	10.7	10.8	
Minneapolis	78	78	93	93	12.1	15.2	91	90	73	72	66	65	0.8	2.4	0.5	0.8	12.5	12.8	12.6	
Newark	69	65	80	87	16.4	14.6	73	73	70	70	51	51	0.6	1.1	1.8	2.1	11.6	10.7	11.4	
Pawtucket	64	68	89	90	8.6	9.9	82	86	72	71	59	61	1.2	2.7	2.4	2.6	11.0	13.2	11.5	
Pittsburgh	75	75	94	95	7.3	10.2	87	87	82	81	71	70	0.9	1.1	0.9	0.7	12.7	9.4	11.9	
Seattle	75	75	92	92	13.5	13.4	80	80	81	81	65	65	1.4	1.1	1.9	1.9	12.7	15.5	13.4	
Tucson	67	64	91	92	4.7	7.3	85	81	69	68	59	55	1.7	2.4	4.1	3.9	10.0	9.2	9.8	
UCDavis	69	70	93	93	12.2	13.8	82	83	71	71	58	59	1.8	3.2	5.8	5.4	10.2	8.9	9.9	

[1] Group dynamics also influence participation. Group dynamics for which we have reports include Timelines of group formation (WHIP 1110 and WHIP 1118) in monthly activity reports.

[2] Women who attended session 12 / women for whom session data have been key-entered. Derived from WHIP0588. Available to CCs through WHIP0427.

[3] % women attending group sessions or completing make-up activities. From WHIP1114. Available to CCs as WHIP0421.

[4] % missed 3 consective sessions (completion) out of women who have been assigned through session 18. From WHIP 1162. Not yet distributed to CCs.

[5] Women who turned in scores for session 12 / women for whom session data have been key-entered. Derived from WHIP0588. Available to CCs through WHIP0423.

[6] % of women with fat scores = or < their fat gram goals. From data analysis not yet routinely distributed to CCs.

[7] (% of women with fat scores = or < their fat gram goals) * (% women with fat scores recorded): % < goal assuming those not reporting a fat score are not meeting the fat gram goal.

[8] From WHIP 748. Not dependent on each other; may stop intervention or follow-up independently.

[9] % AV1 without Intervention - percentage of women who have reached AV1 without having started intervention. From WHIP1134.

[10] [Control-Intervenion] % fat FFQ and 4DFR AV1. Difference between Control and Intervention % fat from FFQ and 4DFR based on AV1 raw data, unadjusted for participant characteristics. Design assumption = 16% at AV1; goal as of AGM 1996 = 13%. Weighted value based on FFQ (0.75) and 4DFR (0.25). The number of AV1 4DFRs is small, thus nutrient data may be unstable. Data not yet routinely distributed.

Table 10.1 (continued)

NCC- DM Intervention - Participation, Adherence, and Retention[1]

	Session Participation						Fat Gram Scores Session 12						% Stop Inter % Stop FU[8]		AV1 w/o Inter[9]		[Cont-Inter]%fat AV1[10]			
	% Attendance Session 12[2]		% Completion Session 12[3]		% Missed 3 Consecutive Sessions[4]		% Collected[5]		% < goal[6]		(% < goal) * (% collected)[7]		FU	Interv			FFQ	4DFR		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., Aug. 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., Aug. 97	cum., Aug. 97	Weighted Value	
Chapel Hill	58	65	81	90	15.6	5.7	65	75	57	64	37	48	0.4	0.3	7.6	8.1	9.7	9.4	9.6	
Chi-Rush	67	66	87	90	5.9	2.3	61	63	62	66	38	42	0.7	0.7	11.4	12.2	9.7	3.5	8.2	
Cincinnati	71	68	95	91	5.1	7.1	83	80	65	66	54	53	0.0	0.0	3.4	4.7	11.7	7.8	10.8	
Columbus	68	67	89	86	6.7	5.7	87	83	66	68	57	56	0.4	0.8	1.8	1.9	12.3	9.5	11.6	
Detroit	60	62	89	87	6.7	4.9	82	79	65	65	53	51	1.6	2.2	5.3	5.3	10.3	17.7	12.2	
Gainesville	72	70	92	91	12.4	13.4	86	86	83	82	71	71	0.3	2.0	3.1	5.2	12.1	8.0	11.1	
GWU-DC	75	75	92	92	5	4.3	86	83	73	73	63	61	1.2	2.8	5.8	5.5	12.4	11.2	12.1	
Honolulu	72	65	87	78	13.3	14.4	74	65	64	65	47	42	0.0	0.3	4.5	5.4	11.3	9.9	11.0	
Houston	66	67	87	87	11.5	15.1	80	83	54	62	43	51	0.0	0.0	3.8	3.5	10.6	8.1	10.0	
Irvine	71	71	81	81	16.7	13.0	75	75	71	70	53	53	1.5	0.0	0.0	2.6	12.3	1.1	9.5	
LA	68	67	91	90	11	14.0	83	81	70	68	58	55	0.8	1.4	4.0	3.4	12.8	0.1	9.6	
Madison	71	72	96	96	1.4	3.0	93	92	73	71	68	65	0.7	1.5	0.0	0.0	13.4	17.1	14.3	
Mediantic	52	52	84	81	13.1	13.7	70	69	61	61	43	42	1.6	4.7	25.0	22.0	7.3	2.7	6.1	
Miami	69	67	94	95	21.1	5.9	88	91	87	86	77	78	0.5	2.9	19.4	24.3	7.7	10.3	8.3	
Milwaukee	77	77	100	100	0	0.0	93	94	75	76	70	71	0.1	0.6	1.2	1.5	12.8	7.1	11.4	
Nevada	77	75	98	97	4.7	5.1	95	95	85	84	81	80	0.7	1.2	0.0	0.6	15.4	24.1	17.6	
NY City	60	64	93	92	5.7	4.1	89	89	55	59	49	53	1.2	1.8	4.3	5.6	9.3	13.2	10.2	
Oakland	81	77	92	88	5.9	4.8	81	80	78	75	63	60	1.2	1.1	3.5	3.1	13.5	11.5	13.0	
Portland	80	80	99	100	0	0.0	94	93	67	67	63	62	0.7	0.6	1.3	1.5	12.2	12.7	12.3	
San Antonio	66	65	93	89	11.4	13.3	86	81	64	60	55	49	1.7	1.4	14.7	16.5	11.1	3.6	9.2	
Stanford	78	75	91	87	4.2	3.8	69	64	77	72	53	46	0.5	0.5	3.4	4.1	11.8	12.8	12.0	
Stony Brook	68	69	97	94	1.6	2.5	93	90	68	69	63	62	0.0	0.8	12.0	9.5	11.5	16.3	12.7	
Torrance	66	68	90	92	1.9	5.8	80	80	73	74	58	59	0.5	1.7	2.7	4.3	13.5	15.6	14.1	
Worcester	77	77	93	94	5.7	2.8	87	87	75	72	65	63	0.6	1.5	3.7	4.6	12.2	12.0	12.1	

[1] Group dynamics also influence participation. Group dynamics for which we have reports include Timelines of group formation (WHIP 1110 and WHIP 1118) in monthly activity reports.

[2] Women who attended session 12 / women for whom session data have been key-entered. Derived from WHIP0588. Available to CCs through WHIP0427.

[3] % women attending group sessions or completing make-up activities. From WHIP1114. Available to CCs as WHIP0421.

[4] % missed 3 consective sessions (completion) out of women who have been assigned through session 18. From WHIP 1162. Not yet distributed to CCs.

[5] Women who turned in scores for session 12 / women for whom session data have been key-entered. Derived from WHIP0588. Available to CCs through WHIP0423.

[6] % of women with fat scores = or < their fat gram goals. From data analysis not yet routinely distributed to CCs.

[7] (% of women with fat scores = or < their fat gram goals) * (% women with fat scores recorded): % < goal assuming those not reporting a fat score are not meeting the fat gram goal.

[8] From WHIP 748. Not dependent on each other; may stop intervention or follow-up independently.

[9] % AV1 without Intervention - percentage of women who have reached AV1 without having started intervention. From WHIP1134.

[10] [Control-Intervention] % fat FFQ and 4DFR AV1. Difference between Control and Intervention % fat from FFQ and 4DFR based on AV1 raw data, unadjusted for participant characteristics. Design assumption = 16% at AV1; goal as of AGM 1996 = 13%. Weighted value based on FFQ (0.75) and 4DFR (0.25). The number of AV1 4DFRs is small, thus nutrient data may be unstable. Data not yet routinely distributed.

Table 10.1 (continued)

CaD Intervention - VCC

	% with Pill Count at SAV-2[1]		% ≥ 80% Adherent at SAV- 2[2]		Adherence Summary at SAV-2[3]		% with Pill Count at AV-2[1]		% ≥ 80% Adherent at AV- 2[2]		Adherence Summary at AV-2[3]		% with Pill Count at AV-3[1]		% ≥ 80% Adherent at AV- 3[2]		Adherence Summary at AV-3[3]		Overall Average	
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97
Atlanta	92	92	55	56	49	50	80	82	60	61	44	48		70		66		43	63	63
Birmingham	97	96	42	42	40	40	87	88	59	57	48	49		81		54		43	62	61
Bowman	91	91	43	48	37	42	86	86	67	67	52	55		86		63		53	63	66
Brigham	86	86	64	63	55	54	82	83	76	73	55	56		77		58		45	70	66
Buffalo	90	90	61	62	52	53	81	82	61	63	46	50		81		69		51	65	67
Chicago	65	65	66	67	40	41	67	71	53	60	30	35		83		57		34	54	57
Iowa	97	97	64	66	62	64	93	93	74	72	64	66		93		67		62	76	75
LaJolla	87	88	67	66	56	56	85	85	67	67	51	54		78		57		43	69	66
Memphis	92	91	48	50	43	44	75	76	58	57	39	41		74		64		45	59	60
Minneapolis	84	85	79	77	65	65	86	87	62	66	50	55		81		51		40	71	67
Newark	64	69	51	51	29	32	87	87	42	46	31	34		72		44		30	51	51
Pawtucket	90	91	52	53	42	43	86	86	52	59	40	48		82		74		56	60	66
Pittsburgh	87	88	63	62	52	52	92	93	61	63	53	57		91		66		52	68	69
Seattle	82	81	62	64	49	50	81	82	57	65	43	51		82		66		50	62	66
Tucson	73	71	53	53	35	35	63	63	59	61	32	34		47		54		23	53	49
UCDavis	88	89	60	59	52	51	84	85	58	60	45	48		73		61		41	65	63

[1] % of visits conducted that include study pill collections or estimates. From WHIP1143.

[2] % of ppts adherent as measured by pill count or estimate at visit. From data analysis not yet routinely distributed to CCs.

[3] % of ppts due for the visit who took at least 80% of their study pills. From data analysis not yet routinely distributed to CCs.

Table 10.1 (continued)

CaD Intervention - NCC

	% with Pill Count at SAV-2[1]		% ≥ 80% Adherent at SAV- 2[2]		Adherence Summary at SAV-2[3]		% with Pill Count at AV-2[1]		% ≥ 80% Adherent at AV- 2[2]		Adherence Summary at AV-2[3]		% with Pill Count at AV-3[1]		% ≥ 80% Adherent at AV- 3[2]		Adherence Summary at AV-3[3]		Overall Average	
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97
Chapel Hill	88	75	57	57	47	40		88		50		37							64	58
Chi-Rush	82	91	43	47	35	43													53	60
Cincinnati	84	85	57	57	46	47	71	84	70	69	47	48							63	65
Columbus	95	95	53	61	46	53		76		79		60							65	70
Detroit	67	75	64	54	36	35		87		54		30							56	56
Gainesville	92	93	61	60	55	55	64	76	68	73	41	54							64	69
GWU-DC	85	86	52	54	44	46	87	80	79	67	63	53							68	64
Honolulu	96	96	58	61	54	55	78	82	57	70	33	57							63	70
Houston	95	93	72	72	56	55	94	93	71	73	53	55							74	73
Irvine	12	15	0	71	0	8													4	32
LA	97	95	47	49	41	39		63		68		37							62	59
Madison	94	93	66	62	62	58		83		77		61							74	72
Mediantic	71	75	62	54	43	37		75		39		25							59	51
Miami	100	94	53	59	32	42		67		50		25							62	56
Milwaukee	97	97	75	71	72	69		90		82		71							81	80
Nevada	93	95	59	62	53	59		78		74		53							68	70
NY City	90	88	54	50	48	44		62		61		36							64	57
Oakland	96	97	67	70	63	67		86		84		70							75	79
Portland	90	87	70	71	60	60		77		63		45							73	67
San Antonio	92	93	70	68	44	44	69	78	56	64	25	36							59	64
Stanford	94	86	65	67	59	54		100		82		78							73	78
Stony Brook	91	91	57	57	51	52		84		63		53							66	67
Torrance	88	90	66	66	55	56		68		70		41							70	65
Worcester	89	90	63	62	56	53		74		55		39							69	62

[1] % of visits conducted that include study pill collections or estimates. From WHIP1143.

[2] % of ppts adherent as measured by pill count or estimate at visit. From data analysis not yet routinely distributed to CCs.

[3] % of ppts due for the visit who took at least 80% of their study pills. From data analysis not yet routinely distributed to CCs.

Table 10.1 (continued)

Outcomes Analysis - VCC

	Form 33 Collection						Documentation						Local Adjudication						Overall Timeliness		
	Form 33: % Collected for CT		Form 33: % Collected for OS[1]		Form 33D: % Collected[2]		% Provider visits for which documents requested[3]		% Cases assigned to local adjudication[4]		% Cases assigned within 6 weeks[5]		% Assigned cases adjudicated		% Adjudicated within 14 days[6]		% Agreement with Central Adj.		% Cases closed within 14 weeks of Form 33[7]		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Atlanta	95	94	91	94	87	83	97	91	71	76	55	46	90	93	82	84			28	29	
Birmingham	97	97	84	84	95	99	97	100	57	59	49	40	63	62	61	57			24	24	
Bowman	88	89	88	90	87	88	86	98	54	73	49	41	66	85	37	50			41	31	
Brigham	97	97	97	96	99	99	89	90	81	78	62	53	95	91	55	48			32	29	
Buffalo	93	94	94	94	97	98	97	98	86	81	83	74	94	96	82	83			54	58	
Chicago	88	86	92	88	88	89	76	72	58	61	48	40	99	98	94	93			30	31	
Iowa	99	99	94	93	95	95	99	98	86	88	63	59	89	95	55	58			33	39	
LaJolla	87	88	88	91	88	92	100	99	88	91	83	82	56	64	34	36			35	48	
Memphis	90	90	88	85	88	85	81	77	74	73	68	66	88	92	65	69			21	27	
Minneapolis	98	98	82	95	90	74	93	93	89	86	77	70	97	90	49	50			47	43	
Newark	87	87	90	91	74	73	94	84	87	73	71	65	91	85	53	50			41	35	
Pawtucket	91	92	86	89	82	85	90	93	88	82	75	74	72	85	58	58			51	44	
Pittsburgh	92	92	47	50	78	82	100	100	92	93	77	78	99	98	86	88			38	41	
Seattle	93	94	95	95	72	84	85	83	80	79	67	62	95	96	86	89			36	40	
Tucson	90	90	93	94	95	96	95	97	81	86	67	62	93	92	60	59			48	50	
UCDavis	92	92	92	94	92	98	91	98	76	90	58	57	100	100	93	95			32	39	

[1] Initial Form 33 mailings from CCC to OS participants was delayed approximately 6 months. From WHIP1257.

[2] Only Form 33, ver. 3 starting March 1996 require Form 33D. From WHIP1257.

[3] Excludes closed cases for which no documents were requested. Derived from WHIP1258.

[4] % cases assigned of those for which documents were requested. Derived from WHIP 1263.

[5] % cases assigned within 6 weeks or have been waiting less than 6 weeks but not yet sent to local adjudication. Derived from WHIP1263 and WHIP1264.

[6] % adjudicated within 14 days or have been waiting less than 14 days but have not yet been adjudicated. Derived fromWHIP1263 and WHIP1264.

[7] % closed within 14 weeks of Form 33 or have been waiting less than 14 weeks from Form 33. Derived from WHIP1262 and WHIP1266.

Table 10.1 (continued)

Outcomes Analysis - NCC

	Form 33 Collection						Documentation						Local Adjudication						Overall Timeliness		
	Form 33: % Collected for CT		Form 33: % Collected for OS[1]		Form 33D: % Collected[2]		% Provider visits for which documents requested[3]		% Cases assigned to local adjudication[4]		% Cases assigned within 6 weeks[5]		% Assigned cases adjudicated		% Adjudicated within 14 days[6]		% Agreement with Central Adj.		% Cases closed within 14 weeks of Form 33[7]		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Chapel Hill	94	94	92	92	80	81	64	87	60	63	56	29	93	98	88	88			61	50	
Chi-Rush	90	94	65	79	58	47	79	88	76	80	61	62	91	85	66	71			59	44	
Cincinnati	91	89	89	89	77	76	89	10	0	0	0	14							31	23	
Columbus	88	90	98	96	73	83	76	75	64	34	43	37	90	88	85	84			52	62	
Detroit	80	75	88	87	5	7													27	35	
Gainesville	97	97	92	91	65	82	84	77	61	73	55	52	91	93	79	83			55	67	
GWU-DC	97	97	93	94	81	78	88	93	60	68	46	51	95	95	94	94			43	39	
Honolulu	94	92	91	89	93	96	100	100	89	90	45	52	95	94	86	89			61	57	
Houston	84	81	86	86	19	21	22	15	73	48	73	48	100	100	100	100			26	27	
Irvine	76	81	88	74		2	73	69	0	0	0	13							15	47	
LA	93	92	95	95	93	96	96	100	47	81	41	45	97	90	80	77			43	47	
Madison	99	98	97	95	99	99	95	97	84	83	79	72	90	97	59	52			82	79	
Mediantic	93	91	67	59	76	66	57	95	46	41	43	34	83	82	43	44			21	11	
Miami	61	73	76	83	16	20	30	70	0	10	36	22							24	38	
Milwaukee	99	98	96	98	99	97	17	85	12	37	23	18	96	64	92	68			44	27	
Nevada	97	97	93	95	96	100	96	100	60	66	25	27	69	76	65	54			39	42	
NY City	96	96	77	82	97	98	97	99	25	30	66	25	67	91	40	59			38	32	
Oakland	95	95	93	93	85	91	78	71	44	44	28	26	84	84	40	33			28	28	
Portland	92	93	90	91	74	74	83	61	49	39	36	47	36	44	36	41			27	23	
San Antonio	71	72	90	89	99	93	85	85	63	70	36	31	96	88	96	90			57	53	
Stanford	94	96	86	93	96	97	99	94	63	67	35	40	89	98	73	74			58	50	
Stony Brook	99	99	94	95	99	95	97	78	74	70	66	62	95	99	86	87			77	72	
Torrance	89	88	93	93	79	83	66	88	9	55	49	33	88	90	100	89			70	35	
Worcester	93	95	93	94	61	83	39	44	31	38	18	25	98	87	98	93			17	44	

[1] Initial Form 33 mailings from CCC to OS participants was delayed approximately 6 months. From WHIP1257.

[2] Only Form 33, ver. 3 starting March 1996 require Form 33D. From WHIP1257.

[3] Excludes closed cases for which no documents were requested. Derived from WHIP1258.

[4] % cases assigned of those for which documents were requested. Derived from WHIP 1263.

[5] % cases assigned within 6 weeks or have been waiting less than 6 weeks but not yet sent to local adjudication. Derived from WHIP1263 and WHIP1264.

[6] % adjudicated within 14 days or have been waiting less than 14 days but have not yet been adjudicated. Derived fromWHIP1263 and WHIP1264.

[7] % closed within 14 weeks of Form 33 or have been waiting less than 14 weeks from Form 33. Derived from WHIP1262 and WHIP1266.

Table 10.1 (continued)

Central Laboratory - VCC

	ECGs % grades 1 - 3[1]		Blood % Complete[2]		4DFRs % < 4 Errors[3]		Summary Average		
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	
Atlanta	91	91	93	93	99	99	94	94	
Birmingham	93	94	96	96	99	99	96	96	
Bowman	91	91	97	97	100	100	96	96	
Brigham	95	95	95	95	96	96	95	95	
Buffalo	95	95	94	94	95	96	95	95	
Chicago	93	93	98	98	99	99	97	97	
Iowa	93	93	98	98	100	100	97	97	
LaJolla	91	91	97	97	98	98	95	95	
Memphis	90	91	88	88	97	97	92	92	
Minneapolis	99	99	100	100	99	99	99	99	
Newark	94	94	97	96	98	98	96	96	
Pawtucket	91	92	99	99	98	97	96	96	
Pittsburgh	91	92	98	98	100	100	97	97	
Seattle	90	91	95	95	94	95	93	94	
Tucson	86	86	93	93	95	95	91	91	
UCDavis	95	95	98	98	95	95	96	96	

[1] % ECGs of acceptable quality (grades 1 - 3). Derived from WHIP1023.

[2] % Complete blood aliquots, based on aliquots required for visit type. From WHIP1044.

[3] % archived 4DFRs with < 4 errors, cum. from Jan. 1, 1995. Derived from WHIP0935. Distributed to CCs quarterly.

Table 10.1 (continued)

Central Laboratory - NCC

	ECGs % grades 1 - 3[1]		Blood % Complete[2]		4DFRs % < 4 Errors[3]		Summary Average	
	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97	cum., May 97	cum., Aug. 97
Chapel Hill	92	92	93	93	100	100	95	95
Chi-Rush	95	95	90	90	90	90	91	92
Cincinnati	96	96	87	86	93	93	92	92
Columbus	95	95	91	91	91	95	92	94
Detroit	92	91	92	92	90	94	92	92
Gainesville	95	95	96	96	85	83	92	91
GWU-DC	89	90	99	99	98	98	95	95
Honolulu	96	96	98	98	98	99	97	98
Houston	95	95	78	78	97	97	90	90
Irvine	97	97	96	96	95	97	96	97
LA	96	96	95	95	100	100	97	97
Madison	96	96	98	98	100	100	98	98
Medlantic	86	87	95	95	89	86	90	89
Miami	94	95	97	97	96	97	96	96
Milwaukee	93	93	95	96	100	100	96	96
Nevada	90	90	99	99	100	100	96	97
NY City	82	83	98	98	87	89	89	90
Oakland	92	92	93	93	98	98	94	95
Portland	97	96	85	85	100	100	94	94
San Antonio	94	94	91	91	94	95	93	93
Stanford	92	92	95	95	100	100	96	96
Stony Brook	92	92	95	95	100	100	95	95
Torrance	92	92	95	95	100	100	96	96
Worcester	95	94	98	98	81	86	91	93

[1] % ECGs of acceptable quality (grades 1 - 3). Derived from WHIP1023.

[2] % Complete blood aliquots, based on aliquots required for visit type. From WHIP1044.

[3] % archived 4DFRs with < 4 errors, cum. from Jan. 1, 1995. Derived from WHIP0935. Distributed to CCs quarterly.

Table 10.1 (continued)

Data Management - VCC

	Timeliness of key-entry[1]		
	cum., May 97	cum., Aug. 97	
Atlanta	95	95	
Birmingham	80	79	
Bowman	91	92	
Brigham	70	71	
Buffalo	97	97	
Chicago	78	80	
Iowa	93	93	
LaJolla	91	91	
Memphis	68	69	
Minneapolis	92	93	
Newark	82	83	
Pawtucket	80	80	
Pittsburgh	86	86	
Seattle	75	76	
Tucson	91	91	
UCDavis	75	74	

[1] Timeliness = % data entered within two weeks. From WHIP1112. Can be run by CC as WHIP0774.

Table 10.1 (continued)

Data Management - NCC

	Timeliness of key-entry[1]		
	cum., May 97	cum., Aug. 97	
Chapel Hill	76	78	
Chi-Rush	67	72	
Cincinnati	74	75	
Columbus	85	86	
Detroit	82	82	
Gainesville	96	96	
GWU-DC	97	97	
Honolulu	87	88	
Houston	85	86	
Irvine	58	61	
LA	78	80	
Madison	98	98	
Medlantic	87	87	
Miami	86	86	
Milwaukee	94	93	
Nevada	97	97	
NY City	87	87	
Oakland	82	83	
Portland	58	61	
San Antonio	93	93	
Stanford	87	87	
Stony Brook	98	98	
Torrance	81	82	
Worcester	87	85	

[1] Timeliness = % data entered within two weeks. From WHIP1112. Can be run by CC as WHIP0774.

11. Study Activities

A number of WHI-related scientific endeavors have been initiated by study investigators. Publications in scholarly journals are approved through the Presentations and Publications Advisory Committee and the Project Office. Ancillary studies are approved by the Design and Analysis Advisory Committee and the Project Office. Those initiatives that could potentially threaten the integrity of the Clinical Trial results before the completion of the study are to be referred to the DSMB for review. A full statement of the relevant policies may be found in the *WHI Manuals, Vol. 1 - Study Protocol and Policies, Section 3 - Study Policies.*

Table 11.1 - Publications presents current and planned publications that have been approved by the Publications and Presentations Committee.

Table 11.2 - Ancillary Studies lists all ancillary study proposals received by the Design and Analysis Committee along with some key features of the studies and their current status.

Table 11.1
Publications

Name of Manuscript	Writing Group	Data Focus	Stage	Publisher
Informed consent in the Women's Health Initiative Clinical Trial and Observational Study	**McTiernan**, Franzi, Johnson, Manson, Nevitt, Rossouw, Taylor, Carleton	Gen.	10	Journal of Women's Health, Vol 4, Num.5
Combined hormone replacement therapy and occurrence of disease in postmenopausal women	**Johnson**, McTiernan, Bachman, Beresford, Dunn, Grady, Judd, Hunninghake, Manson	Gen.	10	
Women's Health and the Women's Health Initiative	**Cochrane**, Hunter, Johnson, Matthews, Strickland, Wactawski-Wende and Woods	Gen.	10	
Book chapter entitled "The Women's Health Initiative: Overview of the nutrition component"...for book titled "Nutrition and Women's Health"	**Tinker**, Burrows, Henry, Patterson, Van Horn, Rupp	Gen.	10	Nutrition & Women's Health, Chapter 18, pp. 510-542, 1996
Women Health Initiative: Why now? What is it? What's new?	**Matthews**, Shumaker, Hunt, Bowen, Klesges, Kaplan, Ritenbaugh, Langer, Weiss	Gen.	10	American Psychlogist, Vol. 52, No. 2, pp. 101-116
Low-fat diet practices of older women: Prevalence and implication for dietary assessment"	**Patterson**, Caggiula, Coates, Kristal, Ritenbaugh, Snetselaar, Stern, Tylavsky, Van Horn	Gen.	10	Journal of the American Dietetic Association
The evolution of the Women's Health Initiative: Perspectives from the NIH"	**Rossouw**, Finnegan, McGowan, Clifford	Gen.	10	Association, Vol. 50, pp. 50-55, 1995
Design of the WHI Clinical Trial & Observational Study	**Prentice**, Rossouw, Furberg, Johnson, Henderson, Cummings, Manson, Freedman, Oberman, Kuller	Gen.	10	Controlled Clinical Trials
Approaches to monitoring the results of long-term disease prevention trials: Examples from the Women's Health Initiative	**Freedman**, Anderson, Kipnis, Prentice, Wang, Rossouw, Wittes, DeMets	CT	10	Controlled Clinical Trials
A comprehensive data management system for multicenter studies	**Anderson**, Davis, Koch	Gen.	9	Controlled Clinical Trials
The role of randomized controlled trials in assessing the benefits and risks of long-term hormone replacement therapy: Example of the Women's Health Initiative	**Prentice**, Rossouw, Johnson, Freedman, McTiernan	CT	9	Menopause, Vol 3, No. 2, pp. 71-76 1996
Factors associated with insurance status among participants in the WHI	**Hsia**, Sofaer, Lillington, Zapaka, Limacher, Kiefe, Sennott-Miller, Mason, Bowen, Kemper	Gen.	8	

Table 11.1 (continued)

Name of Manuscript	Writing Group	Data Focus	Stage	Publisher
Cardiovascular and other physiological correlates of depression	**Wassertheil-Smoller**, Talavera, Campbell, Shumaker, Ockene, Robbins, Dunbar, Greenland, Cochrane	Gen.	8	
Psychosocial and behavioral correlates of moderate alcohol consumption in women	**Powell**, Hymowitz, Criqui, Ockene, Finnegan, Castro, Trevisan, Curb, Hunt, Noonan	CT	8	
Are antioxidants associated with bone mineral density in older women?	**Seeley**, Kritchevsky, Wactawski-Wende, Csuka, Haan, Cauley, Jackson, Caan, LaCriox, Wang	CT	6	
An examination of the differences in total energy and several nutrient scores derived from the FFQ vs estimates based on basal metabolic requirements and Food Record - derived scores in the WHI	**Hebert**, Beresford, Patterson, Chlebowski, St. Jeor, Coates, Elmer, Hartman, Prentice	Gen.	6	
A comparison of health behaviors and health status among lesbian, bisexual and heterosexual women enrolled in the WHI	**Valanis**, Whitlock, Charney, Bassford, Bowen, Carter	CT	5	
The relationship of dietary phytoestrogens menopausal to symptoms and major morbidity in postmenopausal women	**Roman**, Woods, Caggiula, Judd, Brzyski, Liu, Burke, Assaf, Patterson	CT	5	
Body weight and anthropometric measures of adiposity	**Manson,** Kotchen, Perri, Lewis, Johnson, Freed, Hall, Allen, Foreyt, Tinker, Noonan, Stefanick	OS	5	
Correlates of endogenous sex hormone concentrations in WHI	**McTiernan**, Wactawski-Wende, Chen, Meilahn, LaVelleur, Cummings, Hiatt, Baum, Hulka, Wang	CT	5	
Patterns of antihypertensive treatment and control among postmenopausal women	**Wassertheil-Smoller**, Manson, Wong, Lasser, Kotchen, Langer, Grimm, Black, Psaty, Anderson	OS	5	
Prevalence of pelvic organ prolapse and urinary incontinence in women	**Clark**, Nygaard, Harris, Varner, Chang, Hendrix, Barnabei, Maddox, McTiernan, Francis	CT	5	
A comparative analysis of predictors of recruitment for Hispanic and Caucasian women in the WHI	**Talavera**, Fouad, Howard, Satterfield, Schenken, Simon, Porter, Bonk, Hunt, Wang	Gen.	4	

Table 11.1 (continued)

Name of Manuscript	Writing Group	Data Focus	Stage	Publisher
Statistical methods adjusting for restricted population and measurement error	**Wang**, Anderson, Prentice	Gen.	4	Statistics in Medicine
Hormone replacement therapy effects on the resting ECG	**Kadish**, Schwatz, Greenland, Limacher, Frishman, Daughterty, Oberman	CT	4	
Special Populations Recruitment for the WHI: Success and Limitations	**Fouad**, Howard, Lakin, Mouton, Talavera, Thompson, Young, Wang	Gen.	3	
The effects of insurance coverage and ethnicity on mammography utilization in a postmenopausal population	**Bush,** Langer	Gen.	3	
Association between strenuous exercise and alcohol consumption at different stages of life with postmenopausal mental status	**Lindenfeld,** Langer	Gen.	3	
Effects of diet intervention on motivation to make other health related changes	**Lo,** Langer	CT	3	
Completeness of Purchase Mailing Lists for Identifying Older Women	**Falkner**, Wactaski-Wende, Tervisan	CT	3	American Journal of Epidemiology
Comparisons Between Never Smokers, Former Smokers, and Current Smokers in the WHI	**Hymowitz,** Ockene, Bowen, Robbins, Brunner, Shikany, Wagenknecht, Noonan	OS	3	Tobacco Control
Unresolved Issues Regarding HRT: The WHI and its relevance to practicing physicians	**Hall**, Howard	CT	3	Annals of Internal Medicine
Factors Influencing Follow-Up Care for Hypertension and CVD Risk Among WHI Participants in the New York City Area	**Clark**	OS	3	
The Relationship Between Smoking Status, Body Weight, and Waist-to-Hip Ratio: The WHI	**Johnson**, Klesges, Cousins, Manson, Curb, Black, Liu	Gen.	3	
The WHI Dietary Assessment Study	**Patterson,** Kristal, Tinker, Carter, Agurs-Collins, Bolton, Elmer	Gen.	3	
Prevalence of Silent MI	**Sagar,** Kotchen, Hoffman, Wong, Greattinger, Burke, Van Voorhees, Oberman, Taylor	CT	3	

Table 11.1 (continued)

Name of Manuscript	Writing Group	Data Focus	Stage	Publisher
Depression as Mediated by Social Support, Life Events, and Sexual Activity in Postmemopausal Non-Hispanic White and Latina Women	**Larisch,** Talavera, Langer, Velasquez, Elder	Gen.	3	
The relationship of selected dietary components and risk of adenoma and colorectal cancer among postmenopausal women: WHI	**Frank,** Garland, Agurs-Collins, Wylie-Rosette, Paskett, Khandekar, Gams, Shikany	Gen.	3	
Interactions among hormone replacement therapy and dietary fat intake on heart disease risk factors in postmenopausal women	**Chlebowski,** Stefanick, Wagenknecht, Frid, Cain, Mossavar-Rahmani, Fouad	Gen.	3	
The Health Impact of Domestic Violence in Older Women	**Mouton,** Rovi, Schulthiess, Payne, Furniss, Lasser	OS	3	
Determinants of Fasting Hyperinsulinemia	**Manson,** Weidner, LaCroix, Haan, Rodrigues, Wagenknecht, Johnson, Allen, Hendrix	Gen.	3	
Risk of bacterial endocarditis in postmenopausal women undergoing endometrial biopsy	**Limacher,** Barnabei, Smith, Bassford, Schatz, Linn, McNeeley		3	
Sleep complaints: correlates and co-morbidities	**Kripke,** Freeman, Masaki, Brunner, Jackson, Hendrix	CT	3	
Effect of hysterectomy with ovarian preservation on cardiovascular morbidity and mortality	**Brzyski,** Barnabei, Barad, Giudice, Satterfield, Margolis, McNeeley, Taylor	CT	3	
Socio-demographic determinants of folic acid intake	**Beresford,** Heimburger	Gen.	2	
Relationship between adherence to a low fat diet and mental health in women	**Kotchen,** Pluess, Bowen, Hoelscher, Thomson, Schectman, Smith	Gen.	2	
Is a "too low" fat diet a marker of health disease	**Gilligan,** Heimburger	CT	2	
Utility of body mass index (BMI) as a proxy for obesity among White, Black, Asian, Native American and Hispanic postmenopausal women	**Going,** Chen	Gen.	2	
"Patterns of use and characteristics associated with hormone replacement therapy among postmenopausal women"	**Dunn,** Greenland, Lowe, LaCroix	Gen.	2	

Table 11.1 (continued)

Name of Manuscript	Writing Group	Data Focus	Stage	Publisher
A long-term follow-up which would be the relationship of BMD to risk of breast cancer, 5-6 years follow-up would be required	**Cauley,** LaCroix, Lewis	Gen.	2	
The relationship of quality of social support to frequency of cancer screening behaviors among postmenopausal women	**Lane,** Frishman, Taylor, Glanz, Elam, Klaskala, Powell, Messina	Gen.	2	

Type
1= Group authored (no individual names listed)
2=Individual author - study-wide publication
3= Other (local) publication

Stage
2= Approved
3=Analysis proposed
4= Analysis in progress
5= Draft manuscript
6= Final manuscript submitted to P&P Committee
7= Final manuscript approved and sent to WHI Project Office
8= Submitted
9= In press
10= Published

Table 11.2
Ancillary Studies

Study ID#	Title (abbrev.)	Study's Principal Investigator(s)	WHI Investigator	Initial D&A Approval	Initial NIH PO Approval	Funding Status	Active?	ID#s of Other Participating Clinics	Study Population	Sample Size	Speci-mens?	Start Date	Duration	Final D&A approval?	Final NIH PO Approval?	CCC Subcontract/Purchase Services
AS1	ADAPT	John Crouse	Greg Burke	Approved	NA		no	5 CCs	DM	4,000	NA	NA	5 years	NA	NA	NA
AS2	Fat Aversion	Jim Grizzle	Deb Bowen	Approved	yes	dropped	no	12,19,64	WHT women	120	NA	11/1/95	4 years			
AS3	Recruitment Tech.	Kathryn Boe	Robert Langer	Approved		dropped	no	none	NA	400	NA	NA		no	no	no
AS4	Bone Quality in OS	Adrian LeBlanc	John Foreyt	Declined	NA	dropped	no	none	OS	400				NA	NA	NA
AS5	Spinal Stenosis	Lewis Kuller	Lew Kuller	Approved	NA	funded	yes	none	CT	150	NA	ASAP	12 years	yes	N/A	
AS6	Vaginal pH	Anthony Schaeffer	Philip Greenland	Approved	yes	funded	yes	none	HRT	100	vaginal fluid	asap	NA	yes	yes	PS
AS7	Coronary Artery Calcification Detected [illegible]	Judith Hsia	Judith Hsia	Approved	yes	Not an AS	yes	51	OS	782		1/1/97	8 years	yes	yes	no
AS8	Adherence of Older Women	Rowan Chlebowski	Linda Lillington	Approved		under review		none	DM	28	N/A					no
AS9	Hemostatic, Thrombotic, and Genetic Markers	Paul Ridker	David Siscovick	Not an AS		under review		none	OS	1,300	2ml		5 years			
AS10	PLCO-OS	Joel Weissfeld	Lew Kuller	Not an AS	NA		no	1 CC	OS	2,200	NA	NA	WHI	NA	NA	NA
AS11	PLCO-Partners	Joel Weissfeld	Lew Kuller	Not an AS	NA		no	1 CC	DM Partners	NA	NA	NA	NA	NA	NA	NA
AS12	Prostate Cancer-Partners	James Shikany	Al Oberman	Approved	yes	dropped	yes	ALL	DM Partners	10,922	NA	4/1/98	5 years			SC
AS13	Fat Distaste	Pamela Green	Deb Bowen	Approved	NA	dropped	yes	none	DM	160	NA	4/1/95	1.5 years	NA	NA	
AS14	Arthritis	Susan Hughes	Phil Greenland	Approved	NA	dropped	no	none	OS	1,200	NA	1/1/98	5 years	NA	NA	SC
AS15	Ankle/Arm BPI	Lewis Kuller	Lew Kuller	Approved	NA	dropped	no	12, 14, 16, 22, 24, 25, 45	HRT	6,500	NA	asap	9 years		no	
AS16	Partner's Health Study	Robert Langer	Robert Langer	Approved	NA	dropped	no	none	WHI Partners	1,500	NA	7/1/94	15 mos.			
AS17	Urine Metabolites	Elaine Mellahn	Lew Kuller	Approved	yes	dropped	no	All	DM	80,000	NA	7/1/95	5 years	no	no	SC
AS18	Empowerment	Charles Mouton	Norm Lasser	Declined	NA	dropped	no	1 CC	DM	360	NA	7/1/94	4 years	NA	NA	NA
AS19	LEAD & BPI	Mary McDermott	Phil Greenland	Approved	NA	dropped	no	7 CCs	OS	5,500	NA	7/1/95	5 years	NA	NA	
AS20	Coagulation Proteins	Anthony Orencia	Phil Greenland	Approved	NA	dropped	no	21,22,60	OS	782	1.2 ml	NA	4 years	NA	NA	
AS21	EBCT-1 (Coronary Screening)	Robert Detrano	Rowan Chlebowski Harbor UCLA	Approved	NA	dropped	no	63	OS	2,666	NA	2/1/98	2 years	NA	NA	SC
AS22	EBCT-2 (Effect of DM, HRT, CaD)	Robert Detrano	Rowan Chlebowski Harbor UCLA	Approved	NA	dropped	no	2 CCs	CT	2,666	NA	NA	5 years	NA	NA	SC
AS23	Vascular Compliance	Jennifer Robinson	Richard Grimm	Approved	NA	dropped	no	none	CT	500	NA	NA	8 years	no	no	
AS24	NSAIDS	Randall Harris	Rebecca Jackson	Not an AS	NA	dropped	no	ALL	OS	100,000	NA	NA	8 years			
AS25	Knee-Hip OA	James Cerhan	Robert Wallace	Approved	yes	dropped	no	ALL	HRT	11,374	NA	4/1/96	5 years	no	no	SC
AS26	Vitamin D, Calcium, & Breast Cancer	Barbara Hulka	David Sheps	Approved	yes	dropped	no	ALL	ALL	2,600	1.5 ml	12/1/97	5 years			SC

Table 11.2 (continued)

Study ID#	Title (abbrev.)	Study's Principal Investigator(s)	WHI Investigator	Initial D&A Approval	Initial NIH PO Approval	Funding Status	Active?	ID#s of Other Participating Clinics	Study Population	Sample Size	Specimens?	Start Date	Duration	Final D&A approval?	Final NIH PO Approval?	CCC Subcontract/Purchase Services
AS27	Aging	S. Wassertheil-Smoller	S. Wassertheil-Smoller	Approved	yes	dropped	no	none	OS	NA	1.5 ml	NA	5 year follow-up	no	no	no
AS28	Oxidation Status	Michael Gaziano JoAnn Manson	JoAnn Manson	Approved	yes	dropped	no	none	HRT	300	NA	9/1/95	6 months		no	no
AS29	Lung Cancer	Geoffrey Kabat	S. Wassertheil-Smoller	Approved	yes	dropped	no	ALL	OS	87,000	2.5 ml	6/1/96	4 years			SC
AS30	Risk Factors for Fatigue	Arthur Hartz	Jane Kotchen	Approved	yes	dropped	no	21	CT	1,200	NA	1/1/88	3.5 years			PS
AS31	HRT and Mammographic Density	Barbara Hulka	David Sheps	Approved	yes	dropped	no	ALL	HRT	NA	NA		9 years			SC
AS32	Lipid Markers	JoAnn Manson	JoAnn Manson	Declined	NA	dropped	no	12,15,22	OS	NA	NA	9/1/96	NA			
AS33	Hemostatis	Paul Ridker	JoAnn Manson	Declined	NA	dropped	no	12,15,22	OS	NA	NA	9/1/96	NA			
AS34	Metab. Lipoproteins	Joel Morrisett	John Foreyt	Declined	NA	dropped	no	none	All	24	blood	10/1/95	5 years		NA	no
AS35	Insurance	Judith Hsia Shoshanna Sofaer	Valiary Miller	Declined	NA	dropped	no	ALL	OS	All	NA	NA		no	no	no
AS36	Bone Mass	William Goodman	Howard Judd	Declined	NA	dropped	no	none	CT	362	blood, urine	10/1/95	4 years	no	no	no
AS37	RSBD Self-Report in the WHI	James R. Hebert	James R. Herbert	Approved	yes	dropped	no	14, 18, 21, 30, 48, 49, 50, 53,	DM	1,350	NA	6/1/96	2 yesrs			PS
AS38	Prostate & Colorectal Cancer	Albert Oberman	Albert Oberman	Approved	yes	dropped	no	All	DM Partners	34,200	NA	12/1/96	5 yesrs			SC
AS39	ADA- PILOT	Yasmin Rahmani	Yasmin Rahmani	Declined	NA	dropped	no	none	DM		NA		NA	NA	NA	
AS40	Diet & Hormone Dev.	Geoffrey Kabat	Sylvia Smoller	Declined	NA	dropped	no	20	OS	17,500	blood, urine	4/1/97	4 yesrs	NA	NA	NA
AS41	Women & Minority Recruitment	Mona Fouad	Albert Oberman	Declined	NA	dropped	no	none	DM	400	N/A	10/1/96	4 yesrs			
AS42	Predictors of Participation among Latinos	Gregory Talavera	Gregory Talavera	Approved	yes	dropped	no	4	AN	17,270	N/A	9/1/96	4 yesrs	no	no	yes
AS43	Longitudinal Assessment	Beth Ober	Mary Haan	Approved	yes	dropped	no		HRT	110	N/A		6 years			
AS44	Mammography Sensitivity	John Foreyt		Declined		dropped	no		CT	800			3 years			
AS45	Quantitative, Patient-Specific	Joel D. Morrisett, Paul E. Sovelius	John Foreyt	Declined		dropped	no	none	All	5,409	10ml	4/1/97	5 years			no
AS46	Prevalence & Natural History	Margita Zakarija		Declined		dropped	no	none	OS	2,200	6ml	10/1/96	9 years			no
AS47	HRT Decision Project	David Kerner	Robert Langer	Declined		dropped		none	OS	160	N/A					no
AS48	Oral Bone Loss	Cora E. Lewis	Al Oberman	Approved	NA	funded	yes	none	OS	850	NA	7/1/95	7 years	yes	yes	SC
AS49	Sleep and Mood Predictors	Daniel Kripke	Robert Langer	Approved	NA	funded	yes	none	OS	600	urine	6/1/95	5 years	NA	NA	
AS50	HDL Metabolism	Scott Going, Tamsen Bassford	Tom Moon	Approved	NA	funded	yes	none	OS	200	NA	7/1/94	2 years	yes	yes	no
AS51	Osteopenia	Jean Wactawski-Wende	Maurizio Trevisan	Approved	yes	funded	yes	none	OS	1,300	NA	NA	4 years	yes	yes	

Table 11.2 (continued)

Study ID#	Title (abbrev.)	Study's Principal Investigator(s)	WHI Investigator	Initial D&A Approval	Initial NIH PO Approval	Funding Status	Active?	ID#s of Other Participating Clinics	Study Population	Sample Size	Speci-mens?	Start Date	Duration	Final D&A approval?	Final NIH PO Approval?	CCC Subcontract/Purchase Services
AS52	Domestic Violence	Charles Mouton	Norm Lasser	Approved	yes	funded	yes	none	OS	1,000	NA	10/25/94	2 years			
AS53	Skeletal Health	Diane Schneider	Robert Langer	Approved	yes	funded	yes	none	OS	168	NA	1/3/95	2 years			
AS54	Ankle-Arm BPI	Kamal Masaki	David Curb	Approved	yes	funded	yes	none	OS	2,700	NA	7/1/95	2 years			SC
AS55	Eye Care Use	Robert Kleinstein	Al Oberman	Approved	yes	funded	yes	none	OS	300	NA	NA		yes	yes	no
AS56	HRT and Body Fat	Charlotte Mayo	Al Oberman	Approved	yes	funded	yes	none	OS	690	NA	7/31/95	6-9 months	yes	yes	no
AS57	Bone Morphology	Dorothy Nelson	Susan Hendrix	Approved	yes	funded	yes	none	CT	400	NA	5/1/96	4 years	yes	yes	no
AS58	WHI Memory Study	Sally Shumaker	Curt Furberg	Approved	yes	funded	yes	all except #18	HRT	4,800	NA	3/1/96	6 years	yes	yes	SC
AS59	Mammography Behavior	S. Wassertheil-Smoller	Sylvia Wassertheil-Smoller	Approved	yes	funded	yes	none	All	All	NA	NA	NA	yes	yes	no
AS60	Diet & Motivation	Langer/Lo	Langer/Lo	Approved	yes	funded	yes	none	DM	150	NA	5/1/96	1 year	yes	yes	no
AS61	Prostate cancer pilot	Sylvia Smoller	Sylvia Smoller	Approved	yes	funded	yes	none	All	1,607	NA	2/1/96	5 / Mo.	yes	yes	
AS62	ADA- PILOT	Beth Burrows	Ross Prentice	Approved	yes	funded	yes	none	DM	200	NA	10/1/96	1 yr			no
AS63	Behavioral & Psychosocial Predictors	Joan Pfuess	Alice Thomson	Approved	yes	funded	no	none	DM	260	N/A	9/1/96	2 yesrs	yes	yes	no
AS64	Hispanic Women's Advocacy Strategies	Cheryl Kitenbaugh	Cheryl Kitenbaugh	Approved	yes	funded	yes	none	OS	120	N/A	9/1/96	2 yesrs			no
AS65	Prevalence of thyroid problems	Marjita Zakarija	Marianna Baum	Approved	NA	funded	yes	none	OS							
AS66	Diet and prostate CA in WHI spouses	James Shikany	Al Oberman	Approved	yes	funded	yes	none	DM Partners							
AS67	Randomized Controlled Study	Tom Rohan	McTiernan	Approved	yes	funded	no	all	DM	200	N/A		1.5 years			
AS68	The Prevalence of Prognostic Importance	David Sheps	David Sheffield	Approved	yes	funded	yes	10	OS	3,200		7/1/97	3 years	yes	yes	yes
AS69	Retain Women Enrolled In Research	Mona Fouad		Approved		funded		none	DM+HRT	40	N/A	7/1/97	3 months			no
AS70	Age Related Maculopathy	Mary Haan	Mary Haan	Approved	yes	pending submission	no		HRT	3,300	N/A		8 years			
AS71	CVD Risk in Women	Judy Wylie-Rosett		Approved		pending submission	no	none	OS							
AS72	Assessing Stages of Changes	Amy Brewer	Applegate	Declined		pending submission		6	DM	250		7/1/97	8 years			yes
AS73	Body Composition	Zhoa Chen	Cheryl Ritenbaugh	Approved	yes	pending submission		none	OS	800		8/1/97	5 years			yes
AS74	Cultural Differences	Deborah Parra-Medina	Robert Langer & Robert Schenken	Approved	yes	pending submission	yes	3	OS	228	1 drop	5/1/97	1 year	yes	yes	no
AS75	Group Behavior Strategies	Lois Wodarski	Maurizio Trevisan	Approved	yes	pending submission		none	DM	50		7/1/97	3 months		yes	
AS76	Endogenous Sex Hormones	Anne McTiernan	A. McTiernan	Approved	yes	under review	no	All	OS	782	2ml	2/1/97	4 yesrs			NA

Table 11.2 (continued)

Study ID#	Title (abbrev.)	Study's Principal Investigator(s)	WHI Investigator	Initial D&A Approval	Initial NIH PO Approval	Funding Status	Active?	IDits of Other Participating Clinics	Study Population	Sample Size	Speci-mens?	Start Date	Duration	Final D&A approval?	Final NIH PO Approval?	CCC Subcontract/Purchase Services
AS77	Enrollment of Hispanic Women in Trials	Edward Trapido	Marianna Baum	Approved	yes	under review	no	none	All	120	N/A	9/1/96	3 yesrs			no
AS78	Eating Style Index	Pam Haines		Approved	yes	under review	yes		OS	800		9/30/96	2 years		yes	
AS79	Adherence to Dietary Modification	Milagros C. Rosal	Judith Ochene	Decision Pending		under review		6	DM	480		9/1/97	5 years			no
AS80	Ethnicity and Birth Places	Judith Wylie-Rosett	Sylvia Smoller	Approved		under review		none	OS	300	N/A					no
AS81	Combined Effect of HRT	Bruct Psaty	Bruct Psaty	Approved		under review		none	HRT	1,000	1 Allquot	4/1/97	2 years			yes
AS82	Abnormal Androgenic Hair	Ruth Freeman	Sylvia Smoller	Not an AS		under review		none	All	500	N/A					no
AS83	Bone Mineral Density Assessment	Zhao Chen	Cheryl Rifenbaugh	Not an AS		under review		none		200	N/A		4 years			no

OVERVIEW OF MEASURES ON FORMS 37 AND 38 WOMEN'S HEALTH INITIATIVE

This document provides an overview of the measures in Forms 37 and 38 for the Women's Health Initiative. More detailed documentation is available upon request. Investigators should be aware that most of the measures in Forms 37 and 38 were designed for analysis through aggregate scores. Thus, multiple items yield single scores for analyses. Analysis and interpretation of individual items is not appropriate. The CCC staff has detailed information for scoring for all scales. Following are brief descriptions of the concepts and measures. Not all measures described here have defined algorithms.

Depression

Depression is more common among women than among men, but population based studies of depression in postmenopausal women are rare. Measures of depression were included in the WHI to determine whether there is an association between depression, morbidity and mortality. In addition, depression may occur as a consequence of chronic illness. Further, depression may be associated with retention in the study.

Depression is measured in two different ways. In Form 37, there are nine items taken from the medical outcome study, Short Form 36 (Burnman et al, 1988). These items present a brief screening test for depression and mood disorders that have been validated in a large study of office-based practices. In Form 37, these are items 101.1-102.1. In Form 38 they are items 55.1-57.1. These items are a shortened version of the Center for Epidemiological Studies Depression Scale (CES-D). The CES-D has been used in population based studies and has been shown to be a valid and reliable measure of depressed mood (Weissman et al, 1977).

Cognitive Functioning

Cognitive functioning is measured with a modified mini-mental state exam (MMSE). The measurement of cognitive functioning is important because of the keen interest in declines in mental performance with age. Hormone replacement therapy may prevent mental changes in older women although studies are inconsistent. In addition, the complex demands of participation in the WHI may be difficult for women with cognitive limitations. The MMSE is an 18-item interviewer administered test that appears as Items 1-18 in Form 39. The MMSE is commonly used in clinical research studies. It assesses serious problems in mental performance but has less accuracy to detect variations among adults without central nervous dysfunction. This form is only used in women 65 years and older participating in HRT. For more information contact the WHI-MS investigators.

Life Events

A variety of studies have shown that people who have experienced life changes may be more susceptible to chronic illness and to death. Life events are an indicator of life stress. In order to evaluate life events, the WHI includes measures from the Alameda County

Epidemiologic Study (Berkman and Syme, 1979). These items were later modified for the Beta Blocker Heart Attack Trial (BHAT), a study of the post-MI patients (Ruberman et al, 1984). In order to evaluate life events, 11 items with three-point intensity rating were included. These appear as Items 89-99 in Form 37 and Items 44-54 in Form 38.

Social Support

Supportive interpersonal relationships have been shown to be an important predictor of morbidity and mortality. Social support may work in at least two different ways. First, those with good support systems may be more protected from chronic illnesses. The second possibility is that social support may "buffer" stress from life events (Shumaker and Hill, 1991). In order to evaluate social support, a questionnaire from the Medical Outcomes Study has been included in Form 37 (Items 1-9). The questionnaire is designed to assess the amount of social support the patient has available. The nine questions ask respondents to indicate how often each of nine different types of support is available to them. Responses are scored on a five-point scale ranging from "none of the time" to "all of the time." The nine questions form an overall score and four subscales: emotional/informal support, affection, tangible support, and positive social interaction (Sherbourne and Stewart, 1991).

Social Integration

Items 10-14 of Form 37 measure the number and identity of people in one's life and provide an index of how connected the respondent is with other people. Item 10 has seven subcomponents that assess living arrangements. In total there are 12 different questions. The items will be used to evaluate the relationship between social integration and morbidity and mortality. The items were derived from a California Human Population Laboratory, Alameda County study (Berkman, 1984, 1986).

Care Giving

Care giving may be a particular source of social strain and stress for women. As the population ages, more of the women in the study may be assuming care giving roles. Care giving items were included to determine whether these responsibilities predict morbidity and mortality independently of other stress and social support measures. The care giving items were obtained from the Cardiovascular Health Survey (Brown et al, 1990). The information is obtained from a single two-part item in Form 37 (15).

Social Strain

Social relationships may have either positive or negative effects. Social strain is often called "negative social support." For women, strain on existing support systems might interfere with social support and could have a negative effect on health status. Social strain is measured by Items 16-19 in Form 37. The items were obtained from a measure of negative aspects of social relationships developed by Antonucci and colleagues (1989).

Optimism

Optimism represents a cluster of constructs, including perceived control, positive expectations, empowerment, fighting spirit, and lack of helplessness. Some evidence suggests that optimistic people have better outcomes from cardiovascular diseases and cancer. An optimism measure was included in the WHI to evaluate the role of optimistic outlook upon morbidity and mortality. Optimism is measured using a Life Orientation Test-Revised which is a six item scale that appears as Items 20-25 on Form 37 (Scheier and Carver, 1985).

Lack of Expression and Negative Emotions

Some evidence suggests that individuals who are unable to express negative emotions may be more prone to the development or progression of cancer and cardiovascular diseases. In order to assess the relationship between negative emotion and health outcomes, items from the Ambivalence Over Emotional Expression Questionnaire (AEQ) and Emotional Expressiveness Questionnaire (EEQ) are included as Items 26-32 in Form 37 (King and Emmons, 1990).

Hostility

The relationship between hostility and cardiovascular disease has been demonstrated in a variety of studies (Cook and Medley, 1954). Research on the type-A personality has given way to a focus on cynicism and hostility which may be the active components of personality related to heart disease. Hostility is measured using the 13-item cynicism subscale of the Cook-Medley Questionnaire (Cook and Medley, 1954) which appears as Items 33-45 on Form 37. Higher scores on the scale indicate greater levels of hostility (Barefoot et al, 1989).

Quality of Life/Functional Status

Quality of life will be evaluated using a general health status measure. The measure, SF-36 was developed for the medical outcomes study. The SF-36 is perhaps the most widely used health questionnaire in the world today. It has gone through very extensive validity and reliability evaluation. The SF-36 appears as Items 46-83 of Form 37 and as Items 1-38 on Form 38. The SF-36 provides eight quality of life subscales. These include physical functioning (Items 50-59), role limitations due to physical health (Items 63-66), role limitations due to emotional problems (Items 67-69), energy/fatigue (Items 74-78, 80-82), emotional well being (Items 75-77, 79-81), social functioning (Items 60-83), pain (Items 61, 62), and general health (Items 38, 70-73). In each of these subscales, higher scores indicate better health (Ware and Sherbourne, 1992).

Activities of Daily Living

Measures of activities of daily living describe functional independence on a variety of different domains. For the WHI study, four items describing basic activities are included. These appear as Items 84-87 on Form 37 and as Items 39-42 on Form 38.

Symptoms

Much of the minor variation in wellness is captured by reports of symptoms. The WHI questionnaires include lists of symptoms that might be reported by participants. The lists were obtained from the PEPI (Postmenopausal Estrogen/Progestin Intervention) study and from other national health surveys. Thirty-four symptoms are included as Items 88.1-88.34 in Form 37 and Items 43.1-43.34 in Form 38. For scoring, symptoms will be aggregated in several ways. Overall symptoms scores might be calculated. In addition, specific subscores might be used to create an index for HRT and DMT related symptoms (PEPI, 1995; Matthews et al, 1994).

Sleep Disturbance

The aging process is associated with changes in sleep patterns. It is also possible that sleep patterns change as a function of HRT. Sleep is also an important variable in predicting health outcomes and an important aspect of depression in older adults. In the WHI study, sleep is evaluated by Items 103-112 of Form 37 and Items 58-67 of Form 38.

Urinary Incontinence

Urinary incontinence is a significant health problem for older women. Some evidence suggests that estrogen replacement therapy may reduce or eliminate this problem. In order to evaluate urinary incontinence, seven items from the Hormone and Estrogen Replacement Study (HERS) were included. These items appear as number 113-119 on Form 37 and as Items 68-74 on Form 38.

Sexual Functioning

Sexual functioning may be affected by hormonal changes associated with the menopause. Some evidence suggests improvements in vaginal dryness with estrogen replacement therapy. In order to evaluate this issue, five items measuring sexual activity and satisfaction were included. These items appear as number 120-124 on Form 37 and numbers 75-79 on Form 38. The items ask about involvement with a partner, sexual activity, satisfaction, frequency of activity, and worries.

Sexual Orientation

The WHI study includes a single item (Number 125 on Form 37) that assesses sexual orientation. Sexual orientation is included for several reasons. For example, there have been some concerns that women whose sexual partners are primarily other women are at higher risk for breast cancer than are heterosexual women.

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