Women's Health Initiative
Clinical Trial and Observational Study

Annual Progress Report

September 1, 1995 to August 31, 1996

Prepared by
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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, 1996, 32,406 women had been randomized into the CT, representing 11,692 Hormone Replacement Therapy (HRT) randomizations (71% of cumulative goal) and 24,636 Dietary Modification (DM) randomizations (85% 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, 7,390 women have been randomized (67% of cumulative design-based goal). In addition, 42,899 women have be enrolled in the OS.

There has been a concerted effort on the part of CCs with assistance from the Performance Monitoring Committee (PMC) to address recruitment lags. The past six months showed considerable improvement in the overall goals in both VCCs and NCCs. Continued performance at this level will allow us to complete recruitment essentially on schedule for DM and with only a short extension for HRT.

The age distribution has seen a small shift to older age groups. Closing younger age cells to further recruitment on a clinic by clinic basis is beginning to have its impact particularly in VCCs. We anticipate that this approach will eventually give the appropriate balance of women in each age group as it is applied to additional clinics. Minority recruitment has increased and is currently at 18% for the CT.

First year follow-up data indicate that VCCs have conducted 95% of the six month follow-up contacts, 94% of the first annual visit, 89% of the second semi-annual contact, and 90% of the second annual visit. Year 3 visits are now underway at VCCs. Approximately 1% of women have missed two or more consecutive contacts and 1% of randomized women have stopped the usual follow-up procedures.

Adherence to the HRT study appears at this early state to be slightly lower than original projections. Approximately 9.5% of HRT women have discontinued study hormones after an average of approximately 12.4 months on study. Adherence to HRT medications at the first annual visit is between 73% and 85% (defined as percent taking at least 80% of pills). At the second annual visit adherence is between 63% and 85%. Reports of symptoms are common at routine contacts during the first year on study. The HRT Advisory Committee is discussing additional methods of managing these symptoms while encouraging adherence.

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 DM Intervention women are able to follow the intervention program. As noted in the previous report the dietary assessment data available indicate that the baseline percent calories from fat averages based on food records is lower than anticipated (about 34%) and accordingly that the delta achieved at one year is smaller than anticipated (11%). DM Intervention women appear to be meeting or even surpassing their goals for limiting fat intake based on the self-monitoring tools. The analysis of the one year Food Frequency Questionnaires and food records indicate that Intervention women are consuming approximately 23% of energy from fat, as compared to the design value of 21.7%. Thus the Intervention is providing results quite close to target and so the smaller delta is a result of the lower level of fat intake in the controls. In September 1995, the self-monitoring goals were adjusted in an attempt to help achieve the desired intervention effect. Early data suggest this change may increase the delta to about 12% at one year. Further monitoring of this value as well as additional focus on long-term adherence for all and additional assistance for minority women in the Intervention is needed.

Recruitment and adherence in the CaD component has been lower than originally projected. Between 56% and 75% of CT women are entering this component with a likely value in the neighborhood of 65%. Power calculations indicate that a reduction in sample size of this magnitude would not endanger our ability to test the hip fracture and other fractures hypotheses however. Adherence to study supplements is of greater concern as it is clearly lower than expected (with a drop-out rate of 7.9% or 7 months of follow-up on average and a medication rate between 46% and 58% at 6 months post-randomization). The CaD Advisory Committee has recommended several steps to address this, which are being implemented. The effect of these efforts should be available in our next report.

The procedures for documentation and local adjudication of outcomes have been implemented. Central adjudication activities are underway. Listings of outcomes shown in this report are primarily self-reported events. A brief summary of locally adjudicated outcomes is provided. These data are still limited and formal comparisons are not presented here because of their tentative nature.

Current experience indicates some departures from design assumptions particularly for accrual rates, age distribution and early adherence to interventions. A limited examination of study power sensitivity presented previously indicated that these individual deviations cause small reductions in study power (2-3%). Collectively their effects may require some additional design changes if other corrective maneuvers are not successful.

The CC performance monitoring, as previously described, has received considerable attention. The PMC consisting of representatives of the NIH Project Office, the Clinical Coordination Center (CCC) and the Clinical Facilitation Center (Bowman Gray School of Medicine) has been actively reviewing clinic performance, and providing feedback and assistance where appropriate. The focus of these efforts is turning from recruitment toward follow-up and adherence issues. The activities of this Committee are described in this report. A listing of approved publications and of submitted ancillary study proposals is also included.

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, 1995 to August 31, 1996 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 CT component (Hormone Replacement Therapy [HRT], Dietary Modification [DM], and Calcium and Vitamin D [CaD]).

During this period, major emphases included:

- Recruitment into the CT.
- Consideration and preparation for the end of the recruitment period for VCCs without enhanced recruitment.
- Retention and adherence to all CT components.
- Further implementation and tuning of outcomes procedures.
- Continued work by the Performance Monitoring Committee (PMC) to review CC performance and provide assistance where appropriate.
- Initial analyses of baseline data for twelve papers.

All reports summarize Clinical Center (CC) data provided to the CCC by August 31, 1996. Except for the reports of adverse effects, 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 Dr. Valery Miller, Principal Investigator of the NCC at George Washington University, retired in April 1996. Dr. Judith Hsia, previously a Co-Principal Investigator, has assumed the leadership role for this site. We thank Dr. Miller for her work in establishing this site and assuring its excellent start-up.

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 Tuscon and Phoenix, Arizona	Cheryl Ritenbaugh, PhD
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	David Sheps, MD MSPH
CHI-RUSH	Rush Presbyterian- St. Lukes Medical Center and Cook County Hospital 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 Gainseville 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	John Foreyt, 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 Bronx, New York	Sylvia Wassertheil-Smoller, PhD
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 and 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 *Figure 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.

Two NCCs had their recruitment goals reduced: Rush Presbyterian at Chicago (to 50%) and Harbor-UCLA at Torrance (to 75%). 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 original goals within the defined recruitment period. In July the goals for these clinics were changed retroactively to the start of recruitment.

These combined adjustments to clinic goals provide the equivalent of 44.25 clinics recruiting into DM, 45.25 for HRT, and 44.75 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.

Figure 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.
Tuscon	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	
Houston	NCC	50%	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.

Figure 2.2 - Projected and Actual Randomizations at All CCs compares recruitment progress to date for all components by cumulative goals. As of August 31, 1996, 11,692 women had been randomized to HRT (71% of cumulative goal), 24,636 women had been randomized to DM (85% of goal), 7,390 participants had been randomized to CaD (67% of cumulative goal), and 42,899 enrolled into OS (131% of revised cumulative goal). In the last six months accrual has proceeded at 82% of monthly goal for HRT and 98% for DM, as compared to the 65% and 74% observed in the previous six month interval. The retroactive change in goals accounts for 1% of this increase.

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.

VCCs as a group have averaged 260 HRT and 547 DM randomizations per month, an increase of 51 HRT and 138 DM randomizations per month over the previous six month interval. The change in VCC goals during this period was small so this represents a significant improvement in recruitment performance. The VCC monthly accrual rate is now at 75% of goal for HRT and 93% for DM as compared to the previous report of 69% and 83% respectively. The variation between clinics in achieving goals continues to be large, ranging from 59% to 109% of goal for HRT and 73% to 107% for DM. Related clinic performance issues are discussed in *Section 9 - Clinical Center Performance Monitoring.*

In the last six months NCCs recruited at the rate of 364 per month or 79% of their monthly goal for HRT and 708 per month or 88% of goal for DM, bringing them to 65% and 75% of the corresponding cumulative goals. This represents an 11% increase in the cumulative goals during this period. As a group, the NCCs have not yet met the monthly goal for HRT; they were able to exceed the monthly DM goals in August. If these trends continue, NCCs will be able to complete recruitment in the defined recruitment period. The variation in NCC performance is large; for HRT recruitment the range is 34% to 113% of cumulative goal; for DM the range is 36% to 98%. See *Section 9 - Clinical Center Performance Monitoring* for more discussion of clinic specific issues.

Recruitment into CaD began in June 1995 for VCCs and February 1996 for NCCs. *Table 2.2 - CaD Randomization Activity and OS Enrollment Activity by Clinic Group and Month* indicates that in this time 7390 women have been randomized to CaD (6204 in VCCs and 1186 in NCCs), 67% of the uniform accrual based design goal. This represents 56% of those who had been randomized to another CT component as of July 31, 1995 (date selected to allow one additional month for the annual follow-up visit to occur). This figure probably underestimates the true participation rate as some CCs experienced further start-up delays. We note that approximately 75% of women asked to sign a CaD consent form have agreed (see *Table 2.3*) though this value probably overestimates consent since the completion of *Form 11 - Consent Status* may not be complete for women not randomized. The CaD power calculations assume that 70% of CT participants will be accrued into CaD. These data suggest that women may be somewhat less willing to participate in this additional component than expected. The power of the CaD component is robust to rather large changes in sample size, however, so these early results should be viewed cautiously.

OS enrollment in both VCCs and NCCs has progressed well in the last year, with 42,899 women currently participating representing 131% of the revised cumulative goal. (See above discussion of recruitment goals.) The study continues to emphasize CT recruitment over OS; CCs are advised to give priority to scheduling screening visits for potential CT participants.

2.4 Exclusions

Available data on reasons for CT exclusions can be given only a limited interpretation because data entry is not required for women found to be eligible early in the screening process.

The primary reason for excluding age-eligible women from HRT is lack of interest or willingness to be randomized, accounting for approximately 79% of the HRT exclusions. Other exclusions accounting for 1% or more (where a woman can be excluded for multiple reasons) include: not postmenopausal; cancer; clinical assessment of ability to participate; logistical issues; history of DVT; extreme BMI; and recent unexplained weight loss.

The primary reason for excluding women from DM is dietary fat intake, accounting for 46% of the women excluded. Other prevalent exclusions are: lack of interest; large number of meals eaten away from home; cancer; clinical assessment of ability to participate; logistics; not postmenopausal; extreme BMI; recently unexplained weight loss; and age.

Table 2.3 - Reasons for Refusing/Revoking Consent provides further detail on reasons for refusing consent for each consent process (Screening, HRT and DM). See *Form 11 - Consent Status* for the list of reasons for refusing or revoking consent. (Revoking consent in this setting means the woman initially signed a consent and later decided not to participate and hence is not randomized.) Overall, 85% of women at VCCs and 86% at NCCs asked to sign the screening consent have agreed to do so; 29% and 32% of women offered HRT participation at VCCs and NCCs respectively have signed HRT consents. Similarly 61% of VCC women and 63% of NCC women offered DM participation have signed the component-specific consents. CaD consent has been signed by approximately 75% of women approached at VCCs and NCCs though this probably overestimates the proportion consenting as the data may be incomplete for women not participating in CaD.

Among those women who attend a clinic visit but do not consent to screening procedures, commonly reported reasons for not participating include personal issues, study limitations and travel issues. For both HRT and CaD the primary reasons were study limitations, treatments, and worries about symptoms, procedures or risks, and "other." For DM, personal issues, study limitations, and travel were the most frequently identified reasons. The reasons cited have remained quite consistent over time and do not vary substantially between VCCs and NCCs except for some small differences associated with changes in procedures for collecting this information.

2.5 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.

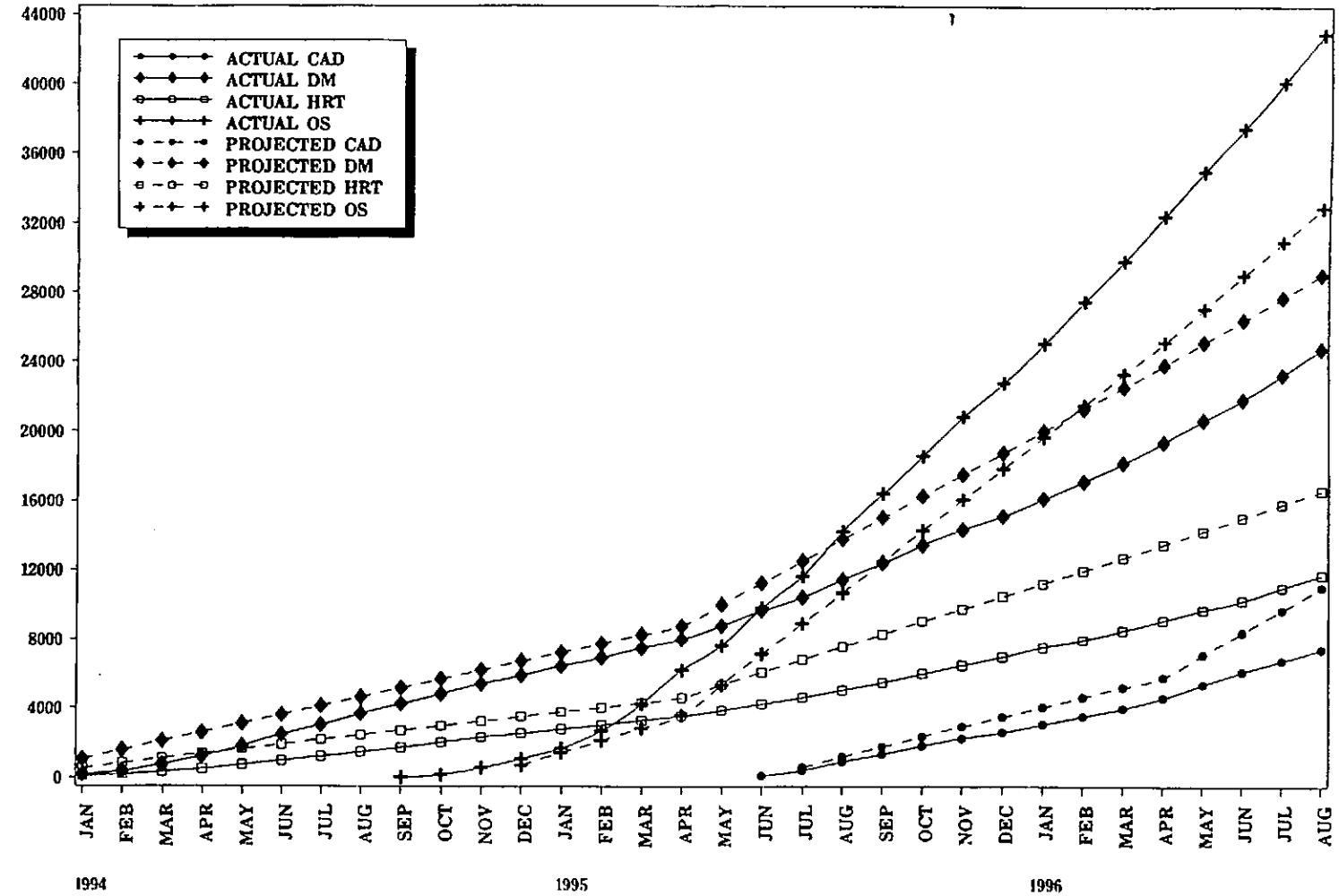
The differential yield and study requirements for HRT and DM have suggested that HRT recruitment could be usefully broadened to a larger catchment area. The clinics that adopted this strategy earlier showed such good results that others have been encouraged to follow suit. An informational brochure useful for HRT only recruitment was developed and recently 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 continues to be a high priority of the study leadership and is discussed frequently in the governing committees. The Steering Committee discusses recruitment issues on a monthly basis. Actions taken by this committee include developing policies for closing recruitment for age cells and extending the recruitment period for HRT and for some VCCs without enhanced recruitment that have the capacity to over-recruit. If these modifications allow us to meet our monthly goals studywide for the duration of recruitment we will reach our total recruitment goals by mid-1998 (5/98 for DM and 7/98 for HRT), only a few months after the original projection.

Figure 2.2

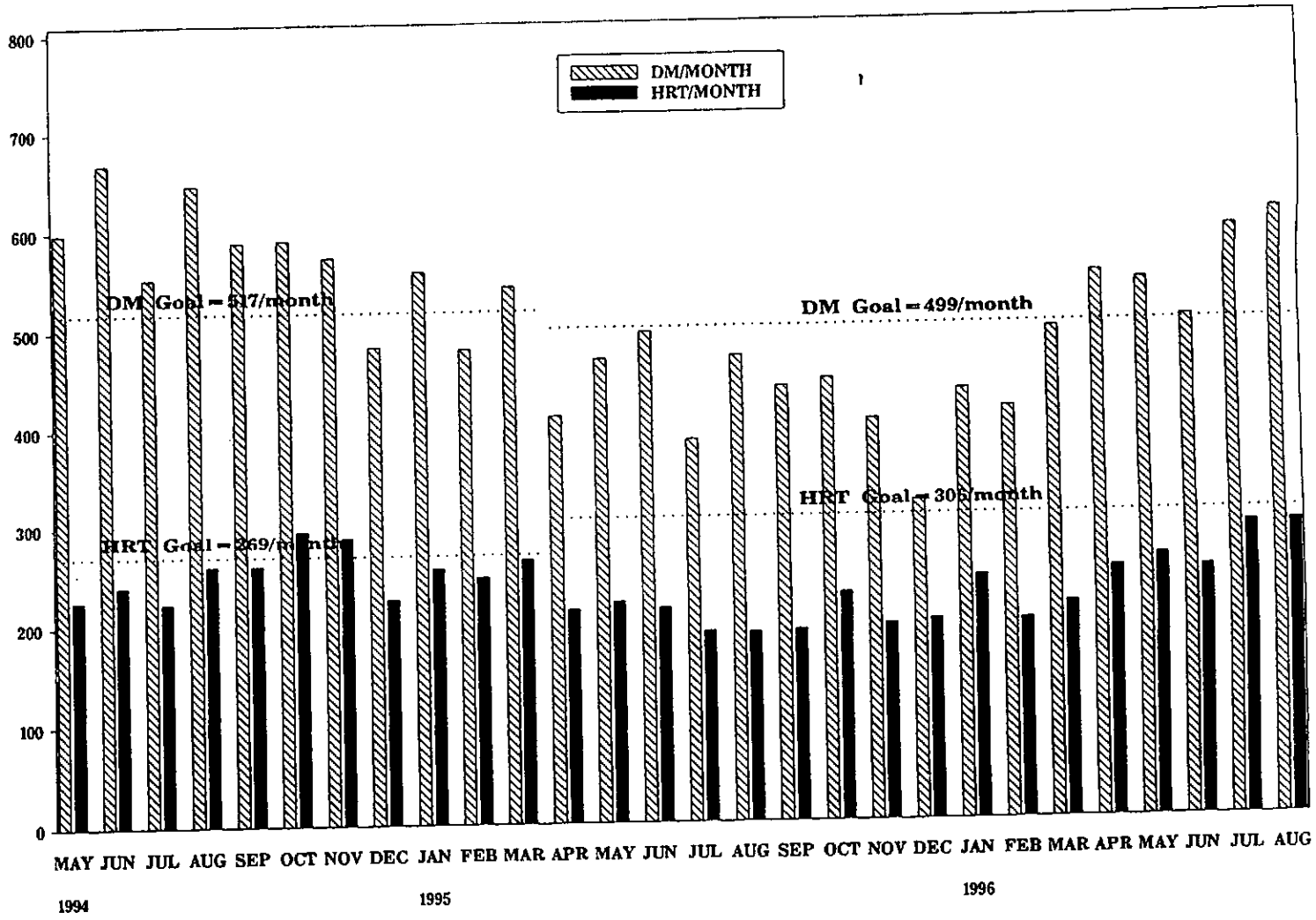
Projected and Actual Randomizations at All CCs



Data as of August 30, 1996

Figure 2.3a

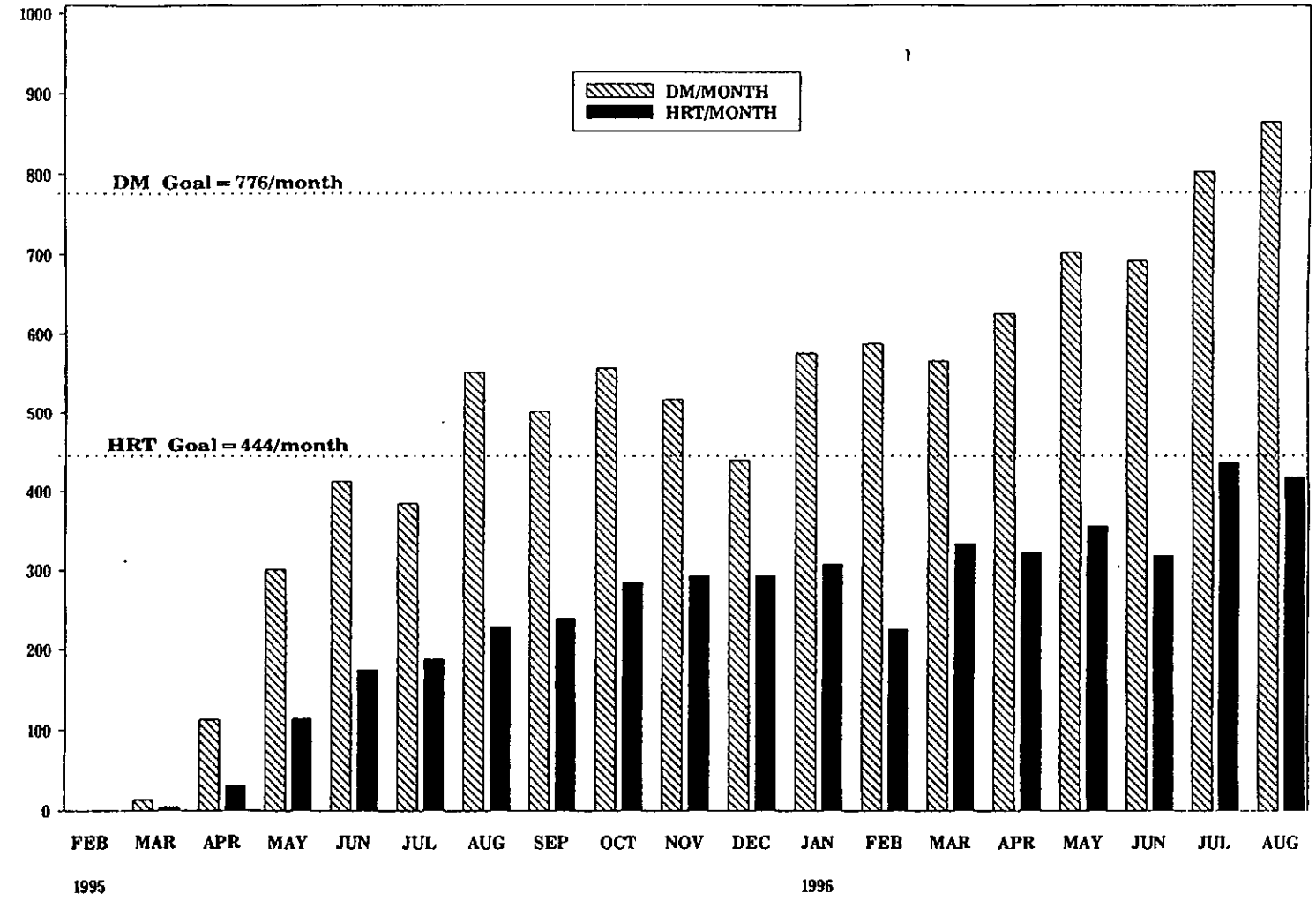
HRT and DM Randomizations per Month at VCCs



Data as of August 30, 1996

Figure 2.3b

HRT and DM Randomizations per Month at NCCs



Data as of August 30, 1996

Table 2.1a
Randomization Activity by Clinic Group, Study Component and Month
Clinic Group: VCC
(Data As Of: 08/30/96)

		HORMONE REPLACEMENT THERAPY RANDOMIZATIONS					DIET MODIFICATION RANDOMIZATIONS					TOTAL CLINICAL TRIAL RANDOMIZATIONS					
Year	Month	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal	CT Number	CT Cum Number	HRT/DM Number	HRT/DM Cum #	Pct Overlap	Pct Cum Overlap
1993	September	0	0	0.0	0.0	0.00%	0	0	0.0	0.0	0.00%	0	0	0	0	0.00%	0.00%
	October	0	0	0.0	0.0	0.00%	1	1	0.0	0.0	0.00%	1	1	0	0	0.00%	0.00%
	November	3	3	0.0	0.0	0.00%	7	8	0.0	0.0	0.00%	8	9	2	2	25.00%	22.22%
	December	30	33	269.4	269.4	12.25%	45	53	517.2	517.2	10.25%	62	71	11	15	20.97%	21.13%
1994	January	65	98	269.4	538.7	18.19%	125	178	517.2	1034.3	17.21%	166	237	24	39	14.46%	16.46%
	February	77	175	269.4	808.1	21.66%	186	364	517.2	1551.5	23.46%	235	472	28	67	11.91%	14.19%
	March	137	312	269.4	1077.4	28.96%	379	743	517.2	2068.7	35.92%	451	923	65	132	14.41%	14.30%
	April	186	498	269.4	1346.8	36.98%	458	1201	517.2	2585.9	46.44%	560	1483	84	216	15.00%	14.57%
	May	226	724	269.4	1616.2	44.80%	598	1799	517.2	3103.0	57.98%	737	2220	87	303	11.80%	13.65%
	June	240	964	269.4	1885.5	51.13%	668	2467	517.2	3620.2	68.15%	806	3026	102	405	12.66%	13.38%
	July	223	1187	269.4	2154.9	55.08%	552	3019	517.2	4137.4	72.97%	671	3697	104	509	15.50%	13.77%
	August	260	1447	269.4	2424.2	59.69%	646	3665	517.2	4654.5	78.74%	799	4496	107	616	13.39%	13.70%
	September	260	1707	269.4	2693.6	63.37%	588	4253	517.2	5171.7	82.24%	745	5241	103	719	13.83%	13.72%
	October	295	2002	269.4	2963.0	67.57%	590	4843	517.2	5688.9	85.13%	763	6004	122	841	15.99%	14.01%
	November	288	2290	269.4	3232.3	70.85%	572	5415	517.2	6206.1	87.25%	750	6754	110	951	14.67%	14.08%
	December	226	2516	269.4	3501.7	71.85%	482	5897	517.2	6723.2	87.71%	613	7367	95	1046	15.50%	14.20%
1995	January	256	2772	269.4	3771.0	73.51%	557	6454	517.2	7240.4	89.14%	715	8082	98	1144	13.71%	14.15%
	February	247	3019	269.4	4040.4	74.72%	479	6933	517.2	7757.6	89.37%	637	8719	89	1233	13.97%	14.14%
	March	264	3283	269.4	4309.8	76.18%	541	7474	517.2	8274.7	90.32%	704	9423	101	1334	14.35%	14.16%
	April	213	3496	306.3	4616.0	75.74%	411	7885	498.6	8773.4	89.87%	553	9976	71	1405	12.84%	14.08%
	May	221	3717	306.3	4922.3	75.51%	467	8352	498.6	9272.0	90.08%	608	10584	80	1485	13.16%	14.03%
	June	214	3931	306.3	5228.6	75.18%	494	8846	498.6	9770.6	90.54%	627	11211	81	1566	12.92%	13.97%
	July	190	4121	306.3	5534.9	74.46%	385	9231	498.6	10269.3	89.89%	508	11719	67	1633	13.19%	13.93%
	August	189	4310	306.3	5841.1	73.79%	469	9700	498.6	10767.9	90.08%	603	12322	55	1688	9.12%	13.70%
	September	191	4501	306.3	6147.4	73.22%	438	10138	498.6	11266.5	89.98%	559	12881	70	1758	12.52%	13.65%
	October	227	4728	306.3	6453.7	73.26%	445	10583	498.6	11765.2	89.95%	599	13480	73	1831	12.19%	13.58%
	November	195	4923	306.3	6760.0	72.83%	404	10987	498.6	12263.8	89.59%	542	14022	57	1888	10.52%	13.46%
	December	199	5122	299.0	7059.0	72.56%	320	11307	487.8	12751.6	88.67%	462	14484	57	1945	12.34%	13.43%
1996	January	242	5364	299.0	7358.0	72.90%	433	11740	487.8	13239.3	88.68%	605	15089	70	2015	11.57%	13.35%
	February	198	5562	299.0	7657.0	72.64%	414	12154	487.8	13727.1	88.54%	559	15648	53	2068	9.48%	13.22%
	March	215	5777	299.0	7956.0	72.61%	493	12647	487.8	14214.8	88.97%	640	16288	68	2136	10.63%	13.11%
	April	249	6026	299.0	8255.0	73.00%	548	13195	487.8	14702.6	89.75%	724	17012	73	2209	10.08%	12.98%
	May	260	6286	301.1	8556.1	73.47%	540	13735	473.5	15176.1	90.50%	713	17725	87	2296	12.20%	12.95%
	June	248	6534	301.1	8857.2	73.77%	502	14237	473.5	15649.6	90.97%	680	18405	70	2366	10.29%	12.86%
	July	292	6826	301.1	9158.3	74.53%	591	14828	473.5	16123.1	91.97%	791	19196	92	2458	11.63%	12.80%
	August	293	7119	301.1	9459.4	75.26%	608	15436	473.5	16596.7	93.01%	822	20018	79	2537	9.61%	12.67%

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Table 2.1b
Randomization Activity by Clinic Group, Study Component and Month
Clinic Group: NCC
(Data As Of: 08/30/96)

		HORMONE REPLACEMENT THERAPY RANDOMIZATIONS					DIET MODIFICATION RANDOMIZATIONS					TOTAL CLINICAL TRIAL RANDOMIZATIONS					
Year	Month	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal	CT Number	CT Cum Number	HRT/DM Number	HRT/DM Cum #	Pct Overlap	Pct Cum Overlap
1995	February	0	0	0.0	0.0	0.00%	0	0	0.0	0.0	0.00%	0	0	0	0	0.00%	0.00%
	March	4	4	0.0	0.0	0.00%	13	13	0.0	0.0	0.00%	16	16	1	1	6.25%	6.25%
	April	31	35	0.0	0.0	0.00%	113	126	0.0	0.0	0.00%	131	147	13	14	9.92%	9.52%
	May	115	150	430.6	430.6	34.84%	301	427	751.5	751.5	56.82%	388	535	28	42	7.22%	7.85%
	June	176	326	430.6	861.1	37.86%	413	840	751.5	1503.0	55.89%	535	1070	54	96	10.09%	8.97%
	July	189	515	430.6	1291.7	39.87%	384	1224	751.5	2254.5	54.29%	514	1584	59	155	11.48%	9.79%
	August	230	745	430.6	1722.2	43.26%	552	1776	751.5	3006.1	59.08%	724	2308	58	213	8.01%	9.23%
	September	240	985	430.6	2152.8	45.75%	501	2277	751.5	3757.6	60.60%	662	2970	79	292	11.93%	9.83%
	October	285	1270	430.6	2583.3	49.16%	557	2834	751.5	4509.1	62.85%	766	3736	76	368	9.92%	9.85%
	November	294	1564	430.6	3013.9	51.89%	517	3351	751.5	5260.6	63.70%	735	4471	76	444	10.34%	9.93%
	December	294	1858	430.6	3444.4	53.94%	439	3790	751.5	6012.1	63.04%	645	5116	88	532	13.64%	10.40%
1996	January	308	2166	430.6	3875.0	55.90%	575	4365	751.5	6763.6	64.54%	789	5905	94	626	11.91%	10.60%
	February	226	2392	430.6	4305.6	55.56%	586	4951	751.5	7515.2	65.88%	744	6649	68	694	9.14%	10.44%
	March	333	2725	430.6	4736.1	57.54%	566	5517	751.5	8266.7	66.74%	806	7455	93	787	11.54%	10.56%
	April	322	3047	430.6	5166.7	58.97%	625	6142	751.5	9018.2	68.11%	850	8305	97	884	11.41%	10.64%
	May	355	3402	474.2	5640.9	60.31%	701	6843	827.7	9845.9	69.50%	941	9246	115	999	12.22%	10.80%
	June	318	3720	474.2	6115.1	60.83%	691	7534	827.7	10673.6	70.59%	911	10157	98	1097	10.76%	10.80%
	July	436	4156	474.2	6589.3	63.07%	802	8336	827.7	11501.3	72.48%	1081	11238	157	1254	14.52%	11.16%
	August	417	4573	474.2	7063.5	64.74%	864	9200	827.7	12329.0	74.62%	1150	12388	131	1385	11.39%	11.18%

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Table 2.2

CaD Randomization Activity and OS Enrollment Activity

By Clinic Group and Month
Data As Of: 08/30/96

Clinic Group: VCC

		CALCIUM AND VITAMIN D SUPPLEMENTATION RANDOMIZATIONS					OBSERVATIONAL STUDY ENROLLMENTS				
Year	Month	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal
1994	September	0	0	0.0	0.0	0.00%	25	25	0.0	0.0	0.00%
	October	0	0	0.0	0.0	0.00%	148	173	0.0	0.0	0.00%
	November	0	0	0.0	0.0	0.00%	374	547	0.0	0.0	0.00%
	December	0	0	0.0	0.0	0.00%	500	1047	700.3	700.3	149.50%
1995	January	0	0	0.0	0.0	0.00%	621	1668	700.3	1400.7	119.09%
	February	0	0	0.0	0.0	0.00%	981	2649	700.3	2101.0	126.08%
	March	0	0	0.0	0.0	0.00%	1091	3740	700.3	2801.3	133.51%
	April	0	0	0.0	0.0	0.00%	1037	4777	767.9	3569.3	133.84%
	May	0	0	0.0	0.0	0.00%	1199	5976	767.9	4337.2	137.78%
	June	118	118	0.0	0.0	0.00%	1010	6986	767.9	5105.1	136.84%
	July	298	416	582.3	582.3	71.44%	880	7866	767.9	5873.0	133.93%
	August	480	896	582.3	1164.6	76.94%	1110	8976	767.9	6641.0	135.16%
	September	415	1311	582.3	1746.9	75.05%	858	9834	767.9	7408.9	132.73%
	October	484	1795	582.3	2329.2	77.07%	840	10674	767.9	8176.8	130.54%
	November	428	2223	582.3	2911.4	76.35%	832	11506	767.9	8944.7	128.63%
	December	353	2576	571.7	3483.1	73.96%	684	12190	773.4	9718.1	125.44%
1996	January	462	3038	571.7	4054.8	74.92%	917	13107	773.4	10491.5	124.93%
	February	462	3500	571.7	4626.4	75.65%	1021	14128	773.4	11264.9	125.42%
	March	467	3967	571.7	5198.1	76.32%	992	15120	773.4	12038.3	125.60%
	April	550	4517	571.7	5769.8	78.29%	1083	16203	773.4	12811.7	126.47%
	May	547	5064	554.8	6324.5	80.07%	1115	17318	828.1	13639.8	126.97%
	June	509	5573	554.8	6879.3	81.01%	1037	18355	828.1	14467.9	126.87%
	July	312	5885	554.8	7434.0	79.16%	1202	19557	828.1	15296.0	127.86%
	August	319	6204	554.8	7988.8	77.66%	1191	20748	828.1	16124.2	128.68%

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Table 2.2 (continued)

Clinic Group: NCC

		CALCIUM AND VITAMIN D SUPPLEMENTATION RANDOMIZATIONS					OBSERVATIONAL STUDY ENROLLMENTS				
Year	Month	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal	Number	Cum. Number	Goal	Cum. Goal	Pct Cum Goal
1995	February	0	0	0.0	0.0	0.00%	22	22	0.0	0.0	0.00%
	March	0	0	0.0	0.0	0.00%	234	256	0.0	0.0	0.00%
	April	0	0	0.0	0.0	0.00%	481	737	0.0	0.0	0.00%
	May	0	0	0.0	0.0	0.00%	932	1669	1017.7	1017.7	164.00%
	June	0	0	0.0	0.0	0.00%	1194	2863	1017.7	2035.4	140.66%
	July	0	0	0.0	0.0	0.00%	1039	3902	1017.7	3053.0	127.81%
	August	0	0	0.0	0.0	0.00%	1345	5247	1017.7	4070.7	128.90%
	September	0	0	0.0	0.0	0.00%	1350	6597	1017.7	5088.4	129.65%
	October	0	0	0.0	0.0	0.00%	1322	7919	1017.7	6106.1	129.69%
	November	0	0	0.0	0.0	0.00%	1389	9308	1017.7	7123.7	130.66%
	December	0	0	0.0	0.0	0.00%	1246	10554	1017.7	8141.4	129.63%
1996	January	0	0	0.0	0.0	0.00%	1323	11877	1017.7	9159.1	129.67%
	February	1	1	0.0	0.0	0.00%	1425	13302	1017.7	10176.8	130.71%
	March	7	8	0.0	0.0	0.00%	1390	14692	1017.7	11194.4	131.24%
	April	68	76	0.0	0.0	0.00%	1483	16175	1017.7	12212.1	132.45%
	May	210	286	750.0	750.0	38.13%	1430	17605	1120.9	13333.0	132.04%
	June	242	528	750.0	1500.0	35.20%	1502	19107	1120.9	14453.8	132.19%
	July	315	843	750.0	2250.0	37.47%	1445	20552	1120.9	15574.7	131.96%
	August	343	1186	750.0	3000.0	39.53%	1599	22151	1120.9	16695.5	132.68%

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Table 2.3

Reasons for Refusing/Revoking Consent

By Study Component and Clinic Group
Data as of: 08/30/96

Clinic Group: VCC

Consent Form Summary

Consent Name	Forms	Signed	%	Refused	%	Revoked	%	Unanswered	%
SCREENING CONSENT	65441	55525	84.85	8662	13.24	1229	1.88	25	.04
HRT CONSENT	32134	9234	28.74	15343	47.75	7525	23.42	32	.10
DMT CONSENT	32266	19581	60.69	5243	16.25	7410	22.97	32	.10
CAD CONSENT	8318	6287	75.58	2027	24.37	0	.00	4	.05

Reason Group	Screening Consent Refused/Revoked		HRT Consent Refused/Revoked		DM Consent Refused/Revoked		CaD Consent Refused/Revoked	
	Count	%	Count	%	Count	%	Count	%
CONFLICTS	115	1.16	742	3.24	102	0.81	30	1.48
CONTACTS	147	1.49	13	0.06	221	1.75	0	0.00
LIMITATIONS	222	2.24	6517	28.50	1506	11.90	251	12.38
LOST CONTACT/DIED	14	0.14	4	0.02	13	0.10	0	0.00
OTHER	4502	45.52	4199	18.36	3638	28.75	389	19.19
PERSONAL	2459	24.86	1114	4.87	3678	29.07	63	3.11
PROCEDURES	78	0.79	53	0.23	228	1.80	0	0.00
REASON NOT GIVEN	1379	13.94	3314	14.49	2714	21.45	689	33.99
REFUSAL	1284	12.98	549	2.40	491	3.88	64	3.16
TRAVEL	644	6.51	393	1.72	970	7.67	5	0.25
TREATMENTS	176	1.78	5097	22.29	169	1.34	521	25.70
WORRIES	81	0.82	2134	9.33	50	0.40	127	6.27

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Table 2.3 (Continued)

Clinic Group: NCC

Consent Form Summary

Consent Name	Forms	Signed	%	Refused	%	Revoked	%	Unanswered	%
SCREENING CONSENT	56617	48783	86.16	7606	13.43	173	.31	55	.10
HRT CONSENT	19656	6359	32.35	10717	54.52	2569	13.07	11	.06
DMT CONSENT	20212	12773	63.20	4177	20.67	3248	16.07	14	.07
CAD CONSENT	1607	1199	74.61	405	25.20	1	.06	2	.12

Reason Group	Screening Consent Refused/Revoked Count	%	HRT Consent Refused/Revoked Count	%	DM Consent Refused/Revoked Count	%	CaD Consent Refused/Revoked Count	%
CONFLICTS	132	1.70	541	4.07	54	0.73	5	1.23
LIMITATIONS	330	4.24	4740	35.68	1087	14.64	57	14.04
OTHER	2664	34.25	1661	12.50	1935	26.06	63	15.52
PERSONAL	2126	27.33	718	5.40	2181	29.37	23	5.67
PROCEDURES	53	0.68	16	0.12	216	2.91	3	0.74
REASON NOT GIVEN	602	7.74	1957	14.73	1435	19.33	106	26.11
REFUSAL	1409	18.11	528	3.97	425	5.72	35	8.62
TRAVEL	955	12.28	331	2.49	617	8.31	5	1.23
TREATMENTS	257	3.30	2809	21.14	221	2.98	105	25.86
WORRIES	25	0.32	622	4.68	31	0.42	23	5.67

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3. Baseline

3.1 Design Parameters and Study Goals

Figure 3.1 - Partial Factorial Design shows the current number of women in each original CT cell under the design (compare to *Figure 1* of the Protocol in the WHI Manuals, *Vol. 1 - Study Protocol and Policies, Section 2 - Protocol*). The numbers originally randomized to ERT and subsequently transitioned to PERT are shown in parentheses under the now closed ERT arm.

Figure 3.1

Partial Factorial Design

Number of women in each cell of the partial factorial design.

DIET			HRT: Intact Uterus: Yes	HRT: Intact Uterus: No	HRT: Not Randomized
			7,004 (331)[1]	4,688	20,714
Intervention		9,867	937 (52)	638	8,292
Control		14,769	1,315 (79)	1,032	12,422
Not Randomized		7,770	4,752 (200)	3,018	—
		32,406			

[1] Randomizations to ERT among women with an intact uterus was stopped on 12/16/94. The number of these women is shown in parentheses.

Age and, for HRT, hysterectomy status are important design factors in determining the required sample size for the CT. *Figure 3.2 - Age Distribution by Study Component and Hysterectomy Status* displays the distribution of age and hysterectomy status by study component. Note that the target age distribution for each component is 10%, 20%, 45% and 25% for the age categories 50-54, 55-59, 60-69, and 70-79, respectively. For HRT, the proportion of randomized women having had hysterectomies at baseline has been modified to reflect the redesign of HRT; the new target is 45%.

The study continues to experience a deficit in the oldest age category; only 18% of HRT participants and 14% of DM participants are 70-79 years of age. This is a 1% increase over the levels reported previously. In the 60-69 year age group the deficits are 4% to 5%. With respect to uterine status, 40% of women randomized to HRT have had hysterectomies.

The difficulties in recruiting older women are numerous. Often these women have multiple health, personal or family issues that create barriers to participation. The long follow-up period had also been reported as a reason these women are reluctant to commit. When these women do attend clinic, the screening process is more difficult for many of the same reasons. To address these recruitment problems systematically, an ad hoc task force, led by Mary Haan, Ph.D. and Co-Principal Investigator at UC Davis and Robert Wallis, MD, Principal Investigator at Iowa developed

recommendations for targeted recruitment of women over 70. These were approved by Council in August and referred to the Clinical Centers and the CCC for implementation.

The policy to close recruitment into the younger age cells at clinics who are nearing or have reached their corresponding goals has been further refined. After updating recruitment projections to reflect recent experience, some modifications were made to permit age-specific recruitment overages at well-performing clinics to make up for the anticipated shortfall at others. Currently for HRT we have closed recruitment at 7 VCCs and 1 NCC for 50-54 year olds. For DM we have closed recruitment at all VCCs and 8 NCCs for 50-54 year olds and 8 VCCs for 55-59 year olds.

Race and ethnicity have been defined to assure the study's ability to address particular questions in minority populations. The study-wide goal to recruit 20% of the WHI population from racial and ethnic minorities (as compared to the 1990 U.S. Census figure of 17%). To achieve this goal, CCs were awarded in two pools: Pool 1 CCs are obliged to recruit 60% of their enrollees (for CT and OS) from racial and ethnic minorities; Pool 2 CCs are asked to recruit minorities in proportion to their local population. Among VCCs, four Pool 1 clinics were named, each with a particular minority population focus: Atlanta (Black/African American); Birmingham (Black/African American); La Jolla (Hispanic); and Tucson (Hispanic/Native American). There are six NCCs identified as Pool 1 clinics: Chicago-Rush (Black/African American); Detroit (Black/African American); Honolulu (Asian/Pacific Islander); Medlantic (Black/African American); Miami (Hispanic); San Antonio (Hispanic). Enhanced recruitment decisions have modified these goals slightly.

Race and ethnicity are determined by self-report on *Form 2/3 - Eligibility Screen* in accordance with the U.S. Census defined categories. *Figure 3.3 - Distribution of Race and Ethnicity* presents the distribution of race and ethnicity among all women randomized or enrolled to WHI by CC group and funding category (Pool 1 or 2).

Among Pool 1 VCCs, 32% of currently recruited women are from racial or ethnic minorities, with most of these being Black/African American (20%) or Hispanic (10%). Among Pool 2 VCCs minority women represent 10% of the accrued population. Among NCCs, Pool 1 sites have recruited 58% of their enrollees from racial or ethnic minorities, 28% Black/African American, 13% Asian/Pacific Islander and 14% Hispanic. Pool 2 NCCs have also recruited over 12% minorities. Minority recruitment in the CT is at 18% overall, and shows a continuing modest increase.

The Special Population Advisory Committee is working with Pool 1 centers, the CCC, NIH and Porter-Novelli to facilitate greater recruitment of minority and lower SES women as well as those over age 70.

3.2 Selected Baseline Predictors

To further characterize the recruited population and to demonstrate the balance achieved on other baseline characteristics, *Table 3.1 - Baseline Characteristics by Study Component* presents the comparisons of selected self-reported baseline variables by study component and by treatment arm.

- Demographic: race/ethnicity; martial status; income; education.

- General Health History: ever smoker; ever drank alcohol.

- Breast Cancer risk factors: age at menarche; parity; age at first pregnancy; family history of breast cancer; history of breast biopsy; oophorectomy status.

- CHD risk factors: history of angina and MI; diabetes; current use of anti-hypertensive medications and cholesterol lowering medications, family history of MI (males and females) before age 55 and at any age.

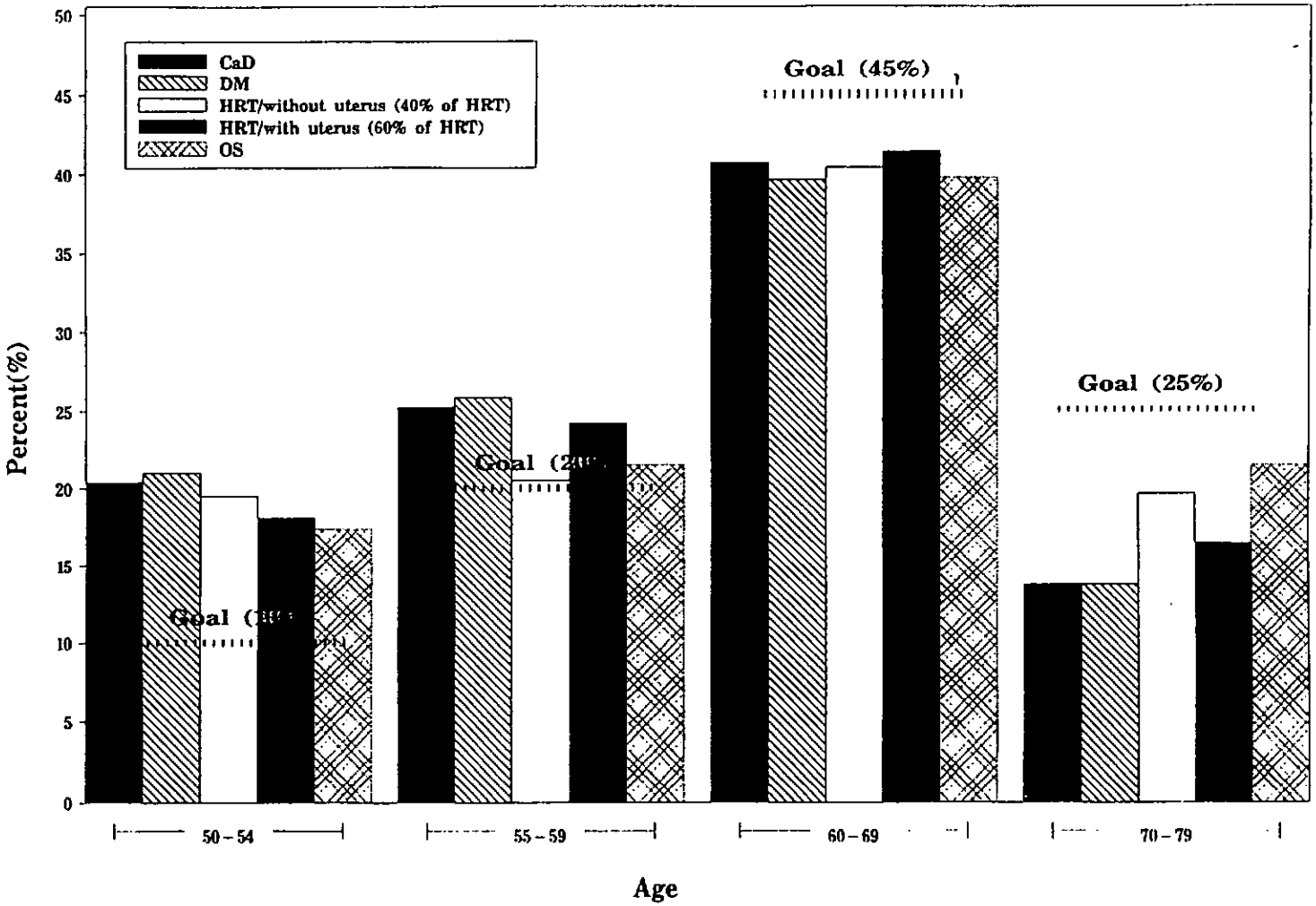
- Fracture risk factors: history of falls, fainting and broken bones.

Table 3.2 - Physical Measures by Study Component shows the similar component specific data for height, weight, body mass index, and systolic and diastolic blood pressures.

The differences between the two HRT cohorts defined by uterine status are of some interest. HRT participants with a uterus are more often white, tend to be of higher SES, lower BMI and blood pressure, and report fewer other key CHD risk factors (history of angina, MI and diabetes, current use of anti-hypertensive medications and some family history of MI). The concern in examining these factors is that the study power for the comparisons within these cohorts is a function of the CHD event rate and differences in baseline risk factors may suggest differential event rates. If the women with a uterus indeed show a lower CHD risk profile, it may become necessary to increase the target fraction of HRT women with a uterus (from 55%) to preserve the power of this treatment comparison. Such a change in goals could be easily implemented since the fraction of women with a uterus in the HRT component currently stands at 60%.

Figure 3.2

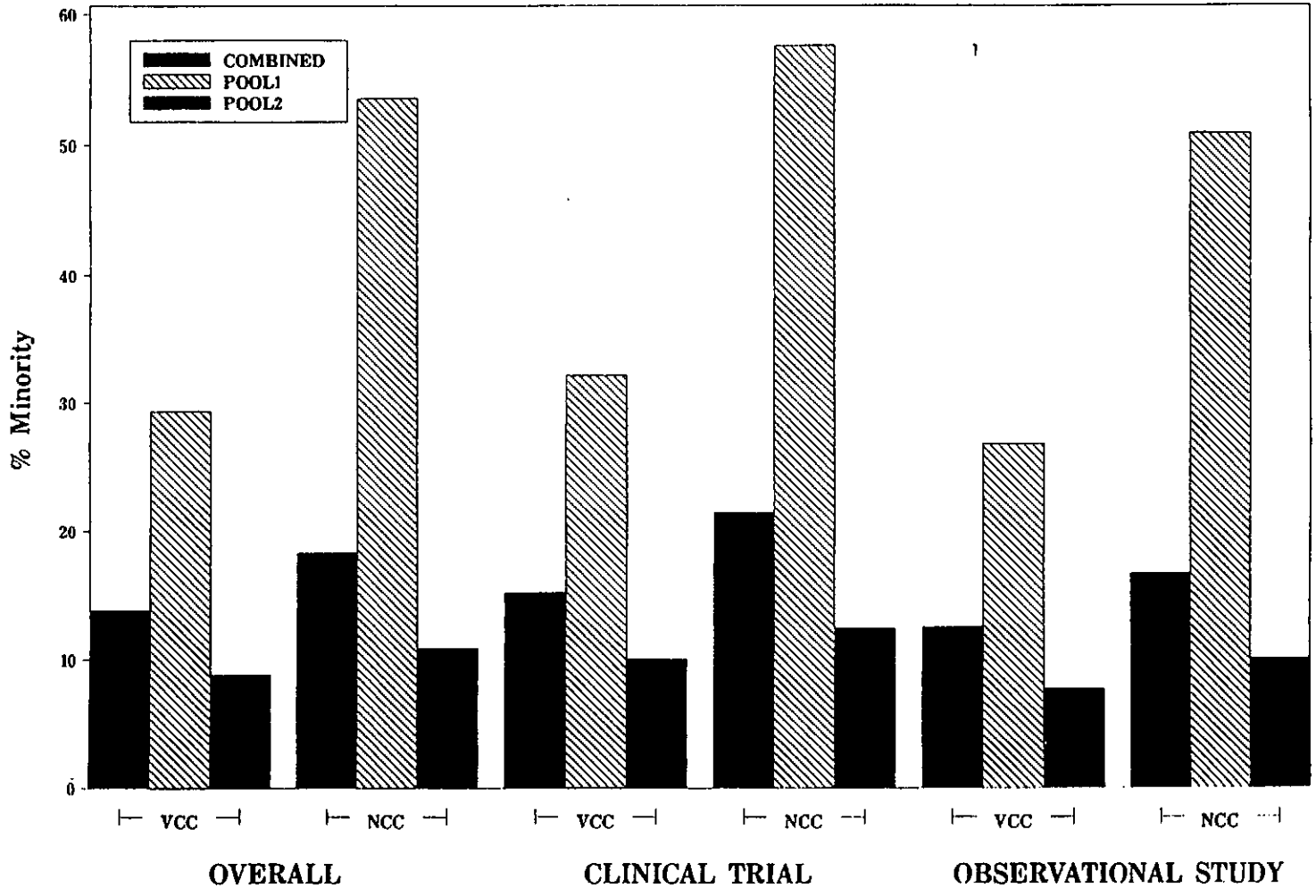
Age Distribution by Study Component and Hysterectomy Status



Data as of August 30, 1996

Figure 3.3

Distribution of Race and Ethnicity



Data as of August 30, 1996

Table 3.1
Baseline Characteristics by Study Component

Demographics Data as of: 08/30/96

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Racial or ethnic group	1	American Indian or Alaskan Native	39	0.8	21	0.3	117	0.5	29	0.4
	2	Asian or Pacific Islander	63	1.3	133	1.9	434	1.8	56	0.8
	3	Black or African-American	753	16.1	475	6.8	2620	10.6	587	7.9
	4	Hispanic	284	6.1	358	5.1	824	3.3	203	2.7
	5	White	3500	74.7	5940	84.8	20372	82.7	6461	87.4
	8	Other	39	0.8	59	0.8	222	0.9	47	0.6
		Value not entered	10	0.2	18	0.3	47	0.2	7	0.1
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Current marital status	1	Never married	145	3.1	306	4.4	1044	4.2	312	4.2
	2	Divorced or separated	184	3.9	261	3.7	789	3.2	498	6.7
	2	Divorced or seperated	741	15.8	958	13.7	3060	12.4	516	7.0
	3	Widowed	903	19.3	1174	16.8	3515	14.3	1108	15.0
	4	Presently married	2620	55.9	4168	59.5	15693	63.7	4823	65.3
	5	Living in a marriage-like relationsh	11	0.2	25	0.4	85	0.3	58	0.8
	5	Marriage-like relationship	56	1.2	88	1.3	351	1.4	53	0.7
		Questionnaire not entered	1	0.0	1	0.0	5	0.0	1	0.0
		Value not entered	27	0.6	23	0.3	94	0.4	21	0.3
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Total family income	1	Less than $10,000	404	8.6	386	5.5	907	3.7	263	3.6
	2	$10,000 to $19,999	852	18.2	975	13.9	2619	10.6	839	11.4
	3	$20,000 to $34,999	1335	28.5	1849	26.4	5717	23.2	1915	25.9
	4	$35,000 to $49,999	866	18.5	1401	20.0	5064	20.6	1559	21.1
	5	$50,000 to $74,999	608	13.0	1157	16.5	4887	19.8	1401	19.0
	6	$75,000 to $99,999	220	4.7	510	7.3	2177	8.8	615	8.3
	7	$100,000 to $149,999	112	2.4	267	3.8	1359	5.5	348	4.7
	8	$150,000 or more	45	1.0	127	1.8	593	2.4	128	1.7
	9	Don't know	113	2.4	141	2.0	562	2.3	135	1.8
		Questionnaire not entered	1	0.0	1	0.0	5	0.0	1	0.0
		Value not entered	132	2.8	190	2.7	746	3.0	186	2.5
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Table 3.1 (Continued)
Baseline Characteristics by Study Component

Demographics Data as of: 08/30/96 (continued)

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Highest grade in school	1	Didn't go to school	10	0.2	5	0.1	12	0.0	5	0.1
	2	Grade school (1-4 years)	44	0.9	53	0.8	70	0.3	28	0.4
	3	Grade school (5-8 years)	99	2.1	105	1.5	222	0.9	75	1.0
	4	Some high school (9-11 years)	299	6.4	279	4.0	757	3.1	246	3.3
	5	High school diploma or G.E.D.	254	5.4	325	4.6	1053	4.3	727	9.8
	5	High school diploma or GED	754	16.1	961	13.7	3142	12.8	662	9.0
	6	Vocational or training school	628	13.4	768	11.0	2463	10.0	723	9.8
	7	Some college or Associate Degree	1379	29.4	1933	27.6	7144	29.0	2117	28.6
	8	College graduate or Baccalaureate	81	1.7	154	2.2	623	2.5	387	5.2
	8	College graduate or Baccalaureate De	271	5.8	542	7.7	2044	8.3	373	5.0
	9	Some college after college graduatio	82	1.7	174	2.5	618	2.5	406	5.5
	9	Some post-graduate or professional	303	6.5	640	9.1	2204	8.9	420	5.7
	10	Master's Degree	373	8.0	880	12.6	3614	14.7	1045	14.1
	11	Doctoral Degree	7	0.1	33	0.5	101	0.4	65	0.9
	11	Doctoral Degree (Ph.D,M.D.,J.D.,etc.	56	1.2	107	1.5	437	1.8	85	1.2
		Questionnaire not entered	1	0.0	1	0.0	5	0.0	1	0.0
		Value not entered	47	1.0	44	0.6	127	0.5	25	0.3
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

General Health History Data as of: 08/30/96

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Smoked 100 cigarettes	0	No	2369	50.5	3393	48.4	12405	50.4	3747	50.7
	1	Yes	2291	48.9	3566	50.9	12084	49.1	3599	48.7
		Questionnaire not entered	2	0.0	8	0.1	22	0.1	13	0.2
		Value not entered	26	0.6	37	0.5	125	0.5	31	0.4
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
12 alcoholic drinks ever	0	No	673	14.4	791	11.3	2505	10.2	776	10.5
	1	Yes	3992	85.2	6182	88.3	22045	89.5	6586	89.1
		Questionnaire not entered	2	0.0	8	0.1	22	0.1	13	0.2
		Value not entered	21	0.4	23	0.3	64	0.3	15	0.2
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Table 3.1 (Continued)
Baseline Characteristics by Study Component

Breast Cancer Risk Factors Data as of: 08/30/96

Short Verbiage	Response Range	HRT w/o Uterus Count	HRT w/o Uterus %	HRT with Uterus Count	HRT with Uterus %	DM Count	DM %	CAD Count	CAD %
Age at first period	10	262	5.6	343	4.9	1262	5.1	365	4.9
	11	714	15.2	1035	14.8	3809	15.5	1090	14.7
	12	1173	25.0	1765	25.2	6407	26.0	1922	26.0
	13	1325	28.3	1969	28.1	7267	29.5	2196	29.7
	14	619	13.2	1032	14.7	3177	12.9	966	13.1
	15	270	5.8	422	6.0	1333	5.4	406	5.5
	16	175	3.7	248	3.5	753	3.1	245	3.3
	17 or older	57	1.2	78	1.1	209	0.8	78	1.1
	9 or less	82	1.7	92	1.3	368	1.5	104	1.4
	Questionnaire not entered	0	0.0	4	0.1	3	0.0	3	0.0
	Value not entered	11	0.2	16	0.2	48	0.2	15	0.2
	Total	4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Response Range	HRT w/o Uterus Count	HRT w/o Uterus %	HRT with Uterus Count	HRT with Uterus %	DM Count	DM %	CAD Count	CAD %
Live births	1	399	8.5	606	8.7	2224	9.0	562	7.6
	2	1029	21.9	1634	23.3	6254	25.4	1729	23.4
	3	1079	23.0	1697	24.2	6028	24.5	1896	25.7
	4	789	16.8	1089	15.5	3714	15.1	1181	16.0
	5	465	9.9	577	8.2	1722	7.0	600	8.1
	6	236	5.0	311	4.4	853	3.5	271	3.7
	7	111	2.4	120	1.7	391	1.6	144	1.9
	8 or more	145	3.1	158	2.3	436	1.8	152	2.1
	None	125	2.7	201	2.9	748	3.0	186	2.5
	Questionnaire not entered	0	0.0	4	0.1	3	0.0	3	0.0
	Value not entered	310	6.6	607	8.7	2263	9.2	666	9.0
	Total	4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Response Range	HRT w/o Uterus Count	HRT w/o Uterus %	HRT with Uterus Count	HRT with Uterus %	DM Count	DM %	CAD Count	CAD %
Age at first term pr	20-24	1838	39.2	2645	37.8	9649	39.2	3082	41.7
	25-29	738	15.7	1456	20.8	5066	20.6	1507	20.4
	30-34	165	3.5	428	6.1	1305	5.3	384	5.2
	35-39	37	0.8	114	1.6	337	1.4	93	1.3
	40-44	7	0.1	24	0.3	66	0.3	17	0.2
	45 or older	0	0.0	1	0.0	2	0.0	0	0.0
	Less than 20	1072	22.9	956	13.6	3432	13.9	1039	14.1
	Questionnaire not entered	0	0.0	4	0.1	3	0.0	3	0.0
	Value not entered	831	17.7	1376	19.6	4776	19.4	1265	17.1
	Total	4688	100.0	7004	100.0	24636	100.0	7390	100.0

Table 3.1 (Continued)
Baseline Characteristics by Study Component

Breast Cancer Risk Factors Data as of: 08/30/96 (continued)

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Female relative breast cancer	0	No	1792	38.2	2683	38.3	9368	38.0	2646	35.8
	1	Yes	763	16.3	1071	15.3	4200	17.0	1243	16.8
	9	Don't know	60	1.3	99	1.4	368	1.5	50	0.7
		Questionnaire not entered	3	0.0	5	0.1	13	0.0	9	0.1
		Value not entered	2070	44.2	3146	44.9	10687	43.4	3442	46.6
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Breast Biopsy Ever		No	3827	81.6	5941	84.8	19955	81.0	6205	84.0
		Yes	836	17.8	1039	14.8	4613	18.7	1168	15.8
		Value not entered	25	0.5	24	0.3	68	0.3	17	0.2
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
One or both ovaries removed	0	No	1919	40.9	6668	95.2	17262	70.1	5249	71.0
	1	Yes, one	133	2.8	53	0.8	362	1.5	242	3.3
	1	Yes, one was taken out	511	10.9	186	2.7	1416	5.7	287	3.9
	2	Yes, both	356	7.6	3	0.0	986	4.0	588	8.0
	2	Yes, both were taken out	1344	28.7	19	0.3	3840	15.6	783	10.6
	3	Yes, unknown number	28	0.6	0	0.0	36	0.1	31	0.4
	3	Yes, unknown number taken out	131	2.8	5	0.1	182	0.7	38	0.5
	4	Yes, part of an ovary	18	0.4	7	0.1	43	0.2	28	0.4
	4	Yes, part of an ovary was taken out	68	1.5	34	0.5	202	0.8	50	0.7
	9	Don't know	151	3.2	9	0.1	226	0.9	67	0.9
		Questionnaire not entered	0	0.0	4	0.1	3	0.0	3	0.0
		Value not entered	29	0.6	16	0.2	78	0.3	24	0.3
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Table 3.1 (Continued)
Baseline Characteristics by Study Component

CHD Risk Factors Data as of: 08/30/96

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Angina	0	No	4349	92.8	6733	96.1	23491	95.4	7082	95.8
	1	Yes	314	6.7	234	3.3	1013	4.1	271	3.7
		Questionnaire not entered	2	0.0	4	0.1	8	0.0	5	0.1
		Value not entered	23	0.5	33	0.5	124	0.5	32	0.4
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Heart attack ever	0	No	4548	97.0	6906	98.6	24268	98.5	7293	98.7
	1	Yes	140	3.0	98	1.4	368	1.5	97	1.3
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Current Antihypertensive Meds		No	3170	67.6	5452	77.8	17627	71.5	5502	74.5
		Yes	1518	32.4	1552	22.2	7009	28.5	1888	25.5
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Current High Cholesterol Meds		No	4333	92.4	6608	94.3	23217	94.2	7002	95.0
		Yes	355	7.6	396	5.7	1419	5.8	368	5.0
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Family History of MI - Any Female		No	2817	60.1	4492	64.1	15875	64.4	4941	66.9
		Yes	1154	24.6	1488	21.2	5331	21.6	1640	22.2
		Don't know	93	2.0	143	2.0	491	2.0	152	2.1
		Value not entered	624	13.3	881	12.6	2939	11.9	657	8.9
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Table 3.1 (Continued)

Baseline Characteristics by Study Component

CHD Risk Factors Data as of: 08/30/96 (continued)

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Family History of MI - Any Female	<55	No	1606	34.3	2335	33.3	8420	34.2	2690	36.4
		Yes	242	5.2	258	3.7	977	4.0	328	4.4
		Don't know	150	3.2	222	3.2	775	3.1	234	3.2
		Value not entered	2690	57.4	4189	59.8	14464	58.7	4138	56.0
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Family History of MI - Any Male		No	2403	51.3	3822	54.6	13211	53.6	4081	55.2
		Yes	1746	37.2	2552	36.4	8972	36.4	2740	37.1
		Don't know	105	2.2	136	1.9	535	2.2	168	2.3
		Value not entered	434	9.3	494	7.1	1918	7.8	401	5.4
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Short Verbiage	Question Response	Response Meaning	HRT w/o Uterus Count	HRT w/o Uterus Pct	HRT with Uterus Count	HRT with Uterus Pct	DM Count	DM Pct	CAD Count	CAD Pct
Family History of MI - Any Male	<55	No	3452	73.6	5477	78.2	18902	76.7	5812	78.6
		Yes	618	13.2	763	10.9	2885	11.7	887	12.0
		Don't know	183	3.9	270	3.9	929	3.8	290	3.9
		Value not entered	435	9.3	494	7.1	1920	7.8	401	5.4
	Total		4688	100.0	7004	100.0	24636	100.0	7390	100.0

Table 3.2
Physical Measures by Study Component

	HRT		DM	CaD	Total
	without uterus	with uterus			
Measure					
Weight (kg)	78.6 (16.5)	74.3 (15.9)	76.3 (15.7)	75.5 (14.6)	75.9 (16.2)
Height (cm)	161.6 (6.8)	161.8 (6.5)	162.4 (6.3)	162.4 (6.0)	162.3 (7.2)
BMI	31.2 (44.7)	28.5 (9.9)	29.5 (23.5)	28.6 (6.0)	29.4 (21.6)
Systolic BP	130.2 (18.2)	127.0 (18.0)	127.2 (17.3)	127.4 (17.2)	127.4 (18.0)
Diastolic BP	77.0 (9.7)	75.9 (9.5)	76.1 (9.4)	76.0 (9.5)	76.1 (9.0)

4. Follow-up and Retention

4.1. Overview

Routine follow-up contacts for the CT are designed to ascertain outcomes, assure safety, and assess and promote adherence to interventions. The follow-up schedule consists of annual clinic visits for all CT women, a semi-annual clinic visit (or contact after year 1) for HRT women and a semi-annual contact (visit, telephone or mail contact at CC discretion) for DM women, and a telephone contact at six weeks post-randomization for HRT women. The Protocol defines a 4-week interval surrounding the anniversary of randomization, or surrounding the six month time point post-randomization as the designated contact window.

4.2. Adherence to Follow-up Procedures

Table 4.1 - Adherence to Follow-up Procedures summarizes adherence to the follow-up protocol by time since randomization and study component. Women are considered to have been due for a contact if the corresponding 4-week contact window was completed by August 31, 1996, indicating that a contact should have occurred.

Current data indicate that approximately 95% of the first semi-annual visits (SAV-1) required to date have been conducted, with 73% occurring within the 4-week window overall; in 95% of these visits all of the required data collection procedures have been completed. For the first annual visit (AV-1), 94% have been conducted, 74% within the four week window and 78% have completed all data collection activities. For the second semi-annual contact (SAV-2), are 89% conducted, 66% in window and 91% complete. The corresponding statistics for the second annual visit (AV-2), are 90% conducted, 68% within window and 83% complete. For the third semi-annual visit we have 75% conducted, 60% within window and 87% complete. This represents a modest improvement in compliance with the procedures, particularly for SAV-2 and AV-2. Though the study strives for complete data whenever practical, the goal for conducting AV-1 is 98%. The current performance, while not yet reaching this goal, represents very high compliance on a whole.

There continue to be small differences in follow-up rates between study components, HRT rates being slightly higher than DM. While small, these differences are likely to persist as women on HRT must attend follow-up visits to stay on their hormones. This linkage between intervention and follow-up does not exist in DM so the perceived need to fulfill study requirements may be less in DM.

Follow-up for women participating in CaD typically begins at SAV-2, six months after their CaD randomization. A small number of women are being randomized at their second annual visit as CaD was not open in time for their AV-1. Their follow-up experience is not reflected in this table.

Clinical Center specific follow-up rates range from 83% to 100% for the SAV-1, 88% to 100% for the AV-1, 66% to 100% for the SAV-2, and 73% to 100% for the AV-2 among VCCs. The improvement seen in some of the more poorly performing clinics may be in part attributed to the focus brought to their issues by the PMC and the corrective actions taken by the CCs. For NCCs the range of performance is expectedly wider and unstable as the numbers are small; many of the

follow-up procedures are still not routine and their primary focus remains recruitment. For SAV-1, the proportion of required contacts conducted ranges from 72% to 100%. For AV-1 the range is 17% to 100% which is a considerable improvement over the previously reported low of 33%. Further discussion of monitoring and improving CC-specific performance may be found in *Section 8 - Clinical Center Performance Summary.*

Completeness of visits is lower than desirable, especially for AV-1 (78%) because of the critical measures of intervention effects collected at this point. Several factors contribute to this including lag time to key entry and assorted data problems, changes in study requirements, and the difficulties in obtaining lab results from outside organizations. Though there has been some improvement in this area, we continue to look for ways to increase our performance. Further streamlining may be required to move this to an acceptable range.

Completeness of visits is greater for DM than HRT, undoubtedly because the number of required procedures are fewer. HRT women are required to have annual mammograms and pelvic exams whereas DM women need only biennial mammography. As many of these activities require requesting information from local providers, there may be a noticeable delay in completing the required activities.

Table 4.2 - Consecutive Missed Contact Summary presents the number of women who have missed their first two, first three, or first four consecutive follow-up contacts. Overall approximately 1% of women due to have these visits have missed all of the required contacts. DM control women are missing consecutive visits twice as often as Intervention women. This difference does not create a significant problem for the study as long as outcome information can still be obtained.

4.3. Retention

Women may refuse to participate in continued intervention or follow-up activities. Women who withdraw from further intervention are strongly encouraged to participate in routine follow-up procedures to promote complete outcome ascertainment. Women who decline Protocol-defined safety related follow-up procedures are to be withdrawn from the intervention. Reports of women changing their participation status post-randomization and associated reasons are to be submitted on *Form 7 - Participation Status.*

Table 4.3 - Participation Status summarizes the current number of women who have asked to stop either their usual follow-up contacts or their intervention by study component and randomization assignment. With an average follow-up time of about 13 months, one percent are not being followed according to the normal procedures, usually at the woman's request. Procedures for maintaining contact, for conducting limited surveillance of health and vital status, and for re-engaging these participants when appropriate are being implemented.

Currently 1107 (9.5%) of the 11,692 women randomized to HRT have discontinued use of study hormones indefinitely. Removing the 331 women who were originally randomized to ERT and moved to PERT, of whom 33% stopped hormones, we would have an intervention drop-out rate of 8.8% with an average of 12.4 months of follow-up, as compared to a design assumption of 6% for 12 months. This may underestimate the true one year drop-out rate because of the large number of

HRT participants with less than one year of follow-up. The drop-out rate among hysterectomized women is 9.9%, somewhat higher than that for women with an intact uterus (7.7% after removing those women who were changed from ERT to PERT by the December 1994 protocol change). In VCCs the drop-out rate is 12.9% with an average of 15.6 months of follow-up. For NCCs the rate is 4.1% with 7.4 months average follow-up time.

For DM, 2.1% of women randomized to the intervention have stopped the intervention activities, with 13 months of follow-up on average.

With only 6.8 months average follow-up, 7.9% of CaD participants are reported as having stopped intervention. If this result persists we would project an annual drop-out rate of 13.4% as compared to the 6% rate assumed in the design.

Table 4.4 - Reasons for Stopping Interventions summarizes the frequency of reported reasons for stopping interventions by study component. The most commonly cited reasons for stopping HRT are: intervention related issues (42%) and health reasons (31%). Personal reasons (35%) were the most often stated among DM stopping intervention, followed by other (36%), intervention (22%) and health reasons (19%). For CaD, intervention related issues are given most often (51%), particularly intervention associated symptoms and dislike of the pills.

Table 4.1

Adherence to Follow-up Procedures

	Number due	Number Conducted	Number Conducted in Window	Number Fully Completed
6-week contact				
HRT	9279	8562 (92%)	6925 (75%)	
SAV-1	**21585**	**20455 (95%)**	**15734 (73%)**	**19432 (95%)**
HRT	7712	7439 (96%)	6243 (81%)	6423 (86%)
DM	16564	15611 (94%)	11662 (70%)	15235 (98%)
Intervention	6640	6283 (95%)	4721 (71%)	
Control	9924	9328 (94%)	6941 (70%)	
AV-1	**13826**	**13021 (94%)**	**10167 (74%)**	**10180 (78%)**
HRT	4788	4555 (95%)	3629 (76%)	3319 (73%)
DM	10865	10210 (94%)	7937 (73%)	8129 (80%)
Intervention	4358	4150 (95%)	3268 (75%)	
Control	6507	6060 (93%)	4669 (72%)	
SAV-2	**8391**	**7446 (89%)**	**5526 (66%)**	**6812 (91%)**
HRT	2885	2633 (91%)	2036 (71%)	2076 (79%)
DM	6691	5891 (88%)	4347 (65%)	5603 (95%)
Intervention	2685	2359 (88%)	1735 (65%)	
Control	4006	3532 (88%)	2612 (65%)	
CaD	3169	2951 (93%)	2266 (72%)	
AV-2	**4039**	**3616 (90%)**	**2734 (68%)**	**2995 (83%)**
HRT	1294	1168 (90%)	877 (68%)	810 (69%)
DM	3295	2947 (89%)	2239 (68%)	2541 (86%)
Intervention	1312	1178 (90%)	903 (69%)	
Control	1983	1769 (89%)	1336 (67%)	
CaD	826	738 (89%)	580 (70%)	

Table 4.1 (continued)

Adherence to Follow-up Procedures

	Number due	Number Conducted	Number Conducted in Window	Number Fully Completed
SAV-3	**333**	**251 (75%)**	**200 (60%)**	**219(87%)**
HRT	133	111 (83%)	95 (71%)	85 (77%)
DM	252	183 (73%)	140 (56%)	164 (90%)
Intervention	97	69 (71%)	54 (56%)	
Control	155	114 (74%)	86 (55%)	
CaD	160	138 (86%)	106 (66%)	

Table 4.2
Consecutive Missed Contact Summary

	Missing SAV-1, AV-1[1]	Missing SAV-1, AV-1, SAV-2[1]	Missing SAV-1, AV-1, SAV-2, AV-2[1]
HRT	**66 (1%)**	**37 (1%)**	**17 (1%)**
DM	**161 (1%)**	**90 (1%)**	**38 (1%)**
Intervention	54 (1%)	24 (1%)	4 (<1%)
Control	107 (2%)	66 (2%)	34 (2%)

[1] Percentage based on those women due for only these contacts.

Table 4.3
Participation Status

	Randomized	Stopped Follow-up	Stopped Intervention
HRT[1]	**11692**	**127 (1%)**	**1107 (9.5%)**
Without Uterus	4688	58 (1%)	462 (9.9%)
With Uterus	7004	69 (1%)	645 (9.2%)
With Uterus and without ERT → PERT	6673	60 (1%)	536 (7.7%)
DM[2]	**24636**	**218 (1%)**	
Intervention	9867	89 (1%)	211 (2.1%)
Control	14769	129 (1%)	
CaD[3]	**7390**	**31 (<1%)**	**582 (7.9%)**

[1] Average follow-up time for HRT participants is 12.4 months.

[2] Average follow-up time for DM participants is 13.0 months.

[3] Average follow-up time for CaD participants is 6.8 months.

Table 4.4

Reasons for Stopping Interventions

Reasons[1]	HRT (N = 1107)	DM (N = 211)	CaD (N = 582)
Personal	61 (6%)	74 (35%)	18 (3%)
Travel	17 (2%)	13 (6%)	2 (<1%)
Study Procedures	17 (2%)	13 (6%)	3 (1%)
Health	340 (31%)	39 (19%)	77 (13%)
Experiencing Health problems or symptom's not due to Intervention	118 (11%)	34 (16%)	50 (9%)
Worried about health effects of medical tests	3 (<1%)	0 (0%)	1 (<1%)
Worried about costs if adverse effects occur	2 (<1%)	0 (0%)	0 (0%)
Advised not to participate by health care provider	145 (13%)	3 (1%)	14 (2%)
Study conflicts with health care needs	117 (11%)	4 (2%)	17 (3%)
Expected more care	7 (1%)	0 (0%)	2 (<1%)
Intervention	460 (42%)	56 (27%)	296 (51%)
Reports health problems or symptoms from WHI intervention	399 (36%)	12 (6%)	207 (36%)
Problem with Clinic Practitioner or other CC staff	6 (1%)	1 (1%)	0 (0%)
Doesn't like taking pills	25 (2%)	2 (1%)	79 (14%)
Doesn't like DM requirements	1 (<1%)	34 (16%)	0 (0%)
Problems with DM group Nutritionist or Group members	2 (<1%)	6 (3%)	1 (<1%)
Doesn't like DM eating patterns	1 (<1%)	19 (9%)	0 (0%)
Doesn't like randomized nature of intervention	25 (2%)	2 (1%)	23 (4%)
Expected some benefit from intervention	14 (1%)	2 (1%)	0 (0%)
Won't participate in safety procedures.	4 (<1%)	0 (0%)	1 (<1%)
Other	249 (23%)	75 (36%)	183 (31%)
Not Given	138 (13%)	30 (14%)	77 (13%)

[1] Multiple reasons may be reported for a woman

5. HRT Intervention Status

5.1 Adherence to Medication

Adherence to medications is assessed by medication rates and changes to study-prescribed hormones. Medication rates are determined by data collected at routine follow-up clinic visits using the actual or estimated number of tablets remaining in the returned bottles and the length of the interval between visits. For this report, women are considered to be adherent to HRT if they have taken 80% or more of their randomized medication for the given interval.

Protocol-defined changes to study medications occur because of hormone related symptoms, other adverse effects or hysterectomy. These changes can be to add progesterone, change to an open-label hormone, or change to another blinded study hormone (from PERT to ERT after a hysterectomy).

Table 5.1 - HRT Adherence Summary presents the proportion of women who were adherent to study hormones (excluding the 331 women with a uterus originally randomized to ERT) by time since randomization and study arm and several demographic and other risk factors. Two approaches were used to handle women for whom pill counts or estimates were not available. The first column assumes that women without a pill count for this time point (9% at SAV-1, 14% at AV-1 and 22% at SAV-2) are non-adherent (taking < 80% of pills), giving an underestimate. The second column presents data limited to those women from whom we obtained a pill count or an estimated count (about 7% of participant gave estimates). Since women who do not come to clinic or who forget to bring their bottles may be less adherent than average, this latter number may be an overestimate. This implies that the six month adherence rate is between 82% and 90%, and the annual rate is between 73% and 85%, essentially unchanged from our last report. Year 2 rates are between 68% and 88% at SAV-2 and between 63% and 86% at AV-2.

Under the best case scenario, adherence rates have decreased only 4.5% from SAV-1 to AV-2. The number of women missing pill counts has increased from 8.6% to 26% during this interval which suggests that the decline in adherence may be steeper.

Education and ethnicity have a strong effect on adherence with lower adherence among minority women and those women having eight or fewer years of education as does the performance of the 6-week phone contact. Age and hysterectomy status are not strong predictors of adherence.

As an additional measure of pill-taking and participant tracking we have looked at the number of women who are still considered active in the study but have not had pills dispensed with in the last 215 days (one bottle's-worth of pills). Of the 6,442 women who are active and have been randomized for at least 215 days, 254 (3.9%) have not had a bottle dispensed within the last 215 days. The variability between CCs indicates this may be a tracking issue. Eight VCCs and 14 NCCs have fewer than 3% of women missing medications whereas one VCC and six NCCs have greater than 9%.

Finally, as was noted in *Section 4.3 - Retention* and *Tables 4.3* and *4.4*, 1107 (9.5%) HRT women have discontinued study medications entirely. The primary reasons given for stopping study medications were aspects of the intervention (42%) and health issues (31%).

Adherence to HRT was the primary focus of the May 1996 meeting for CC clinic practitioners, gynecologists, and Principal Investigators. Early identification of potential adherence problems and coping strategies were presented. Further discussion is planned for the November 4 - 5 Annual General Meeting. In addition, the PMC has begun to target their monitoring and site visits to those clinics whose participants exhibit poorer adherence.

5.2 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.

Bleeding is a common problem for women with an intact uterus in the first year on study. *Table 5.2 - Reports of Bleeding* presents the number of reports of bleeding among women with a uterus by contact type. Twenty-four percent reported bleeding at their six week contact, 30% at SAV-1, 20% at AV-1, 16% at SAV-2, 14% at AV-2 and 15% at SAV-3.

Table 5.3 - Other HRT Symptoms summarizes the breast changes at the 6 week, semi-annual and annual visits and at non-routine contacts. Note that a delay in implementing the data collection procedures for these symptoms reduces the available sample size compared to other displays. Reports of breast changes (new lumps, nipple discharge or skin changes) are slightly higher in hysterectomized women than in women with a uterus at all follow-up time points. While 8% to 10% of women are reporting these symptoms at 6 weeks, by AV-1 the prevalence is reduced to 3% to 4% by AV-1 and appears to be levelling off.

5.3 Unblinding

Unblinding to the HRT randomization assignment is indicated for management of severe symptoms and for serious adverse effects. See WHI Manuals, *Vol. 2 - Procedures, Section 5.4 - Managing Symptoms, Section 5.5 - Major Health Problems* and *Section 5.6 - Unblinding* for details. As of August 31, 1996, 563 (4.8%) HRT participants' assignment had been unblinded. The primary reason for unblinding is persistent bleeding at 6 months post-randomization. In these instances, the protocol allows for the consulting gynecologist to be unblinded to better assess the need for an endometrial aspiration. The remaining cases represent unblinding for other symptoms, medical conditions, provider request and clinic error, 56 cases in total.

5.4 Laboratory Monitoring

The endometrial monitoring plan for HRT has been modified to reflect the revised HRT design. In the new plan, 5-6% of women with a uterus will have an endometrial aspiration at follow-up years 3, 6, and 9. Initially all ERT women with a uterus were to have aspirations annually. Since only a small number of HRT participants had reached their annual visit before the change in protocol, there are very few results available for routine monitoring (see *Table 5.4 - Results of Endometrial Monitoring*). At AV-1, hyperplasia was present in 9 (5%) of women biopsied (8 cystic, 1 adenomatous). Abnormalities occurred among 31 (9%) women having unscheduled biopsies. Nineteen of the 31 cases of cystic hyperplasia and all of the adenomatous cases occurred in women with a uterus originally randomized to ERT (see *Section 5.5 - ERT to PERT Transition*).

5.5 ERT to PERT Transition

By December 16, 1994, 331 non-hysterectomized women had been randomized to ERT. In January 1995, these women were personally contacted by the clinic and informed of the change in protocol. The CCC also sent information to all HRT participants regarding this change. Beginning in February 1995 and as soon thereafter as the local IRB approvals were in place, these women were transitioned to PERT. The transition required several steps including signing a new consent, having an endometrial aspiration if on ERT for eight or more months, taking MPA 10mg for 30 days and then changing to the PERT arm. All of these 331 women were unblinded but no other HRT participants were unblinded as a result. Clinics made every reasonable effort to keep all staff except the Clinic Practitioner blinded to these women's randomization assignments.

The initial response of these women to the change was positive and accepting. After the transition began, however, many women experienced symptoms, particularly bleeding. Though this was expected, many women have found it troublesome. To date 109 (33%) of these women have discontinued their assigned hormones.

Endometrial aspirations performed for these women (85 at AV-1, 129 unscheduled) have yielded 26 positive results (see *Table 5.4*): 19 with cystic hyperplasia, 5 with adenomatous hyperplasia and 2 having adenomatous hyperplasia with atypia. These results were included in the discussion above, accounting for all but thirteen of the abnormalities.

Table 5.1
HRT Adherence Summary

	All HRT Participants[1]		Participants with Pill Counts[1]	
	N	% Adherent[2]	N	% Adherent
SAV-1	**7381**	**81.8**	**6748**	**89.5**
Age				
50-54	1350	78.4***	1210	87.4**
55-59	1670	81.5	1522	89.4
60-69	3079	83.8	2840	90.8
70-79	1282	81.2	1176	88.5
Ethnicity				
Minority	1350	71.6***	1174	82.4***
White	6016	84.1	5561	91.0
Education				
0-8 Years	208	69.7***	177	81.9***
Some H.S. or diploma	1835	80.7	1678	88.3
Any school after H.S.	5280	82.7	4840	90.2
Hysterectomy				
No	4293	82.6*	3937	90.1
Yes	3088	80.7	2811	88.7
Had 6-week Call[3]				
No	427	64.9***	336	82.4***
Yes	6015	83.1	5563	89.8
AV-1	**4457**	**73.3**	**3825**	**85.4**
Age				
50-54	780	70.9	670	82.5
55-59	953	73.9	814	86.5
60-69	1965	74.6	1707	85.8
70-79	759	71.5	634	85.6
Ethnicity				
Minority	705	61.8***	571	76.4***
White	3746	75.4	3248	86.9
Education				
0-8 Years	126	56.3***	97	73.2**
Some H.S. or diploma	1154	71.8	973	85.2
Any school after H.S.	3152	74.6	2736	86.0
Hysterectomy				
No	2502	74.3	2156	86.2
Yes	1955	71.9	1669	84.2
Had 6-week Call[3]				
No	293	55.6***	213	76.5***
Yes	3225	74.8	2804	86.1

*p < 0.05; ** p < 0.01; *** p < 0.001

[1] Excludes 331 ERT-PERT participants and includes participants that stopped intervention/meds.
[2] If no collection then considered < 80% adherent.
[3] Only includes participants randomized after 7/15/94.

Table 5.1 (continued)
HRT Adherence Summary

	All HRT Participants[1]		Participants with Pill Counts[1]	
	N	% Adherent[2]	N	Adherent
SAV-2	**2254**	**68.4**	**1993**	**87.7**
Age				
50-54	459	64.7*	349	85.1
55-59	528	68.0	405	88.6
60-69	1149	71.1	920	88.8
70-79	418	65.8	319	86.2
Ethnicity				
Minority	352	61.6**	263	82.5**
White	2200	69.5	1728	88.5
Education				
0-8 Years	73	53.4*	50	78.0
Some H.S. or diploma	674	69.3	526	88.8
Any school after H.S.	1797	68.8	1409	87.7
Hysterectomy				
No	1341	71.0**	1068	89.1*
Yes	1213	65.6	925	86.1
Had 6-week Call[3]				
No	171	52.6***	112	80.4*
Yes	1444	70.7	1166	87.6
AV-2	**1125**	**62.7**	**827**	**85.2**
Age				
50-54	182	58.8	126	84.9
55-59	267	61.8	194	85.1
60-69	521	65.1	398	85.2
70-79	155	60.6	109	86.2
Ethnicity				
Minority	132	55.3	94	77.7*
White	991	63.7	731	86.3
Education				
0-8 Years	39	38.5**	25	60.0***
Some H.S. or diploma	303	64.0	235	82.6
Any school after H.S.	780	63.6	567	87.5
Hysterectomy				
No	587	65.2	440	87.0
Yes	538	59.9	387	83.2
Had 6-week Call[3]				
No	25	40.0	13	76.9
Yes	161	58.4	113	83.2

*p < 0.05; ** p < 0.01; *** p < 0.001

[1] Excludes 331 ERT-PERT participants and includes participants that stopped intervention/meds.
[2] If no collection then considered < 80% adherent.
[3] Only includes participants randomized after 7/15/94.

Table 5.2

Reports of Bleeding

Data as of: 08/30/96

	with Uterus
6 Week HRT Phone Call	
Number with an HRT Safety Interview	5763
Number with Bleeding	1403 (24.3%)
Semi-Annual Visit 1	
Number Having Visit	4470
Number with Bleeding	1323 (29.6%)
Annual Visit 1	
Number Having Visit	2701
Number with Bleeding	530 (19.6%)
Semi-Annual Visit 2	
Number Having Visit	1544
Number with Bleeding	240 (15.5%)
Annual Visit 2	
Number Having Visit	689
Number with Bleeding	95 (13.8%)
Semi-Annual Visit 3	
Number Having Visit	71
Number with Bleeding	11 (15.5%)
Non Routine Visit	
Number Having Visit	7004
Number with Bleeding	759 (10.8%)

Table 5.3

Other HRT Symptoms

Data as of: 08/30/96

	without Uterus	with Uterus
6 Week HRT Phone Call		
Number with an HRT Safety Interview	3794	5763
Number with Breast Changes	307 (8.1%)	562 (9.8%)
Semi-Annual Visit 1		
Number with an HRT Safety Interview	2876	4286
Number with Breast Changes	180 (6.3%)	331 (7.7%)
Annual Visit 1		
Number with an HRT Safety Interview	1805	2631
Number with Breast Changes	69 (3.8%)	122 (4.6%)
Semi-Annual Visit 2		
Number with an HRT Safety Interview	1029	1431
Number with Breast Changes	26 (2.5%)	53 (3.7%)
Annual Visit 2		
Number with an HRT Safety Interview	500	714
Number with Breast Changes	17 (3.4%)	28 (3.9%)
Semi-Annual Visit 3		
Number with an HRT Safety Interview	51	79
Number with Breast Changes	2 (3.9%)	5 (6.3%)
Non Routine Visit		
Number with an HRT Safety Interview	4688	7006
Number with Breast Changes	26 (0.6%)	85 (1.2%)

Table 5.4
Results of Endometrial Monitoring

	With Uterus[1]	ERT to PERT
AV-1		
No endometrial tissue	24 (13%)	7 (8%)
Insufficient specimen	19 (1%)	9 (11%)
Normal atrophic endometrium	67 (35%)	26 (31%)
Normal secretory endometrium	2 (1%)	2 (2%)
Normal proliferative endometrium	53 (28%)	28 (33%)
Cystic hyperplasia present	8 (4%)	5 (6%)
Adenomatous hyperplasia present	1 (1%)	1 (1%)
Other	4 (2%)	2 (2%)
Value not entered	12 (6%)	5 (6%)
AV-2		
Insufficient specimen	5 (19%)	1 (8%)
Normal atrophic endometrium	12 (46%)	7 (58%)
Normal proliferative endometrium	7 (27%)	3 (25%)
Other	1 (3.8%)	1 (8%)
Value not entered	3 (12%)	1 (8%)
Non-Routine		
No endometrial tissue	30 (9%)	16 (12%)
Insufficient specimen	24 (7%)	13 (10%)
Normal atrophic endometrium	111 (32%)	50 (39%)
Normal secretory endometrium	10 (3%)	4 (3%)
Normal proliferative endometrium	100 (29%)	44 (34%)
Cystic hyperplasia present	21 (6%)	13 (10%)
Cystic hyperplasia with atypia	2 (1%)	1 (1%)
Adenomatous hyperplasia present	4 (1%)	4 (3%)
Adenomatous hyperplasia with atypia	2 (1%)	2 (2%)
Atypia Present	1 (<1%)	0
Cancer Present	2 (1%)	0
Other	16 (5%)	9 (7%)
Value not entered	23 (7%)	9 (7%)

[1] Includes women transitioned from ERT to PERT. ERT-to-PERT women account for all of the adenomatous hyperplasias and 19 of the 31 cases of cystic hyperplasia.

6. DM Modification Intervention Status

6.1 Timeliness of Intervention

Because the Dietary Modification intervention is delivered in a group format, the first major hurdle in conducting the DM Intervention is starting groups. Ideally, all women in the Intervention arm should start attending group sessions within 12 weeks of randomization. Waiting times of 20 weeks or more are a concern because of the lesser amount of intervention that can be delivered before the first Annual Visit. Once randomized, the CC nutritionists make monthly contacts (phone or mail) with DM Intervention participants to discuss group starting times. Women waiting four weeks receive a copy of *Your New Eating Style*, a brief overview of the intervention.

Table 6.1 - Timeliness of Intervention Group Formation describes the waiting time for women to begin their first intervention session by clinic group. Currently 7,605 (77%) of the 9,867 women randomized to DM Intervention have begun sessions. Of these 10% waited 20 weeks or more for their first session. Of the 2,262 women waiting to begin sessions, 19% have waited 20 weeks or more. Of the women randomized to DM Intervention who have reached their first annual visit 136 (3.0%) have not started intervention (data not shown).

Table 6.1
Timeliness of Intervention Group Formation

	VCC		NCC		Total	
Randomized to Intervention	6172		3695		9867	
Intervention Started	5146	(83%)	2459	(66%)	7605	(77%)
Waited ≥ 20 weeks	517	(10%)	248	(10%)	765	(10%)
Awaiting Intervention	1026	(17%)	1236	(34%)	2262	(23%)
Waiting ≥ 20 weeks	231	(22%)	191	(16%)	422	(19%)

6.2 Adherence to the Intervention Program

Adherence to the DM intervention is assessed by a variety of methods including attendance to group intervention sessions, completing make-up sessions, and by self-monitoring reports of fat, fruit, vegetable, and grain scores. Sessions 4, 8, and 12, and 16 are used as indicators of performance during year one of the intervention.

Table 6.2 - Intervention Program Adherence Summary describes the performance of DM Intervention women at these four sessions. Attendance is relatively high over the first 6 (weekly) sessions with 85% attending Session 4. When the sessions move to every other week beginning at Session 7, attendance declines to 78% at Session 8, 70% at Session 12 and 68% at Session 16. Experience from the Women's Health Trial suggests that attendance will decline when the time interval between sessions becomes longer. However, attendance in the WHT was found to be positively correlated with attaining fat intake goals, emphasizing the value of promoting attendance.

Completion is defined as session attendance after taking into account make-up sessions. Make-up sessions may be completed by attending a different group or by individual or group sessions with a group nutritionist. The effect of make-up compared to regular group attendance on attaining intervention goals is unknown. Individual make-up sessions do increase staff workload and clinics are encouraged to minimize the need for individual make-up sessions. Approximately 90% of make-up sessions are conducted individually or in small groups other than guest attendance at regular sessions. Completion is above 90% for Sessions 4, 8, and 12, indicating that make-up sessions increase over time.

Another measure of intervention participation is the number of consecutive sessions that participants miss, which discriminates between occasional and sequential absences. Of the 3,535 women who have been assigned to all 18 sessions of the year 1 intervention, 7.4% have missed 3 or more consecutive sessions (data not shown). Additional data for 4-8 missed consecutive sessions are as follows: 5.6% for 4 or more sessions, 4.6% for 5 or more sessions, 3.6% for 6 or more sessions, 2.9% for 7 or more sessions, and 2.4% for 8 or more sessions. Note that consecutive missed session data are reported cumulatively, i.e., participants missing eight sessions are also counted as missing seven, six, five, four, and three sessions. When participants miss 3 consecutive sessions the nutritionists activate a restart plan (Interrupted Participation) with participants to partake in as much of the intervention as possible and ultimately attend sessions again.

Self-monitored fat gram scores are collected and recorded at each session beginning with Session 3 so that participants and nutritionists can track progress toward the goal. The CCC monitors fat scores collected at Sessions 4, 8, 12, and 16, with the expectation that participants should have attained their fat gram goals by Session 8. Nutritionists provide additional assistance, at a minimum after Sessions 8, 12, and 16 to women exceeding their fat gram goals by 25% (i.e., at 125% or greater of their goal). Performance of self-monitoring was also found to be correlated positively with attending sessions and attaining fat intake goals in the WHT so it is important for participants to maintain self-monitoring.

Self-monitoring scores were obtained from 93% of participants at Session 4, 88% at Session 8, 84% at Session 12, and 80% at Session 16. Because missing values are potential indicators of poorer adherence, the complete collection of these data is a priority. Among those women with scores available, the average reported fat score was lower than the average goal beginning at Session 4 and continuing through Session 18 (data not shown). At Session 12, 75% of women who reported scores were less than their goal and 90% were within 5 grams of achieving their goal (within approximately 25% of goal, data not shown).

Self-monitored fruit/vegetable and grain scores are collected and recorded at each session beginning at Session 8 so that participants and nutritionists can track progress toward the goal. The CCC monitors fruit/vegetable and grain scores at Sessions 8, 12, and 16, with the expectation that participants should have attained their fruit/vegetable goal of 5 servings per day by Session 12 and their grain goal of 6 servings per day by Session 16. Over 84% of women provided fruit/vegetable and grain scores at Session 12. The average scores were 5.5 servings per day of fruit and vegetable and 5.1 servings per day of grain.

On average, 2.1% of the women randomized to the DM Intervention have stopped participating in the intervention (see *Section 4.3*). The major reasons given for stopping intervention include personal, the intervention itself, health, and other.

Table 6.3 - Intervention Program Adherence Summary - Participants with Revised (Lower) Fat Gram Goals displays the performance of DM Intervention who received lower fat gram goals per protocol change in implemented September 15, 1995. (The rationale for this protocol change is described in *Section 6.3 - Comparison of Dietary Intake.)* Approximately 4,144 women have been assigned to fat gram goals from the revised algorithm. Of these, 818 have had the opportunity to attend Intervention sessions through Session 16. Over 90% of these women completed fat scores at Sessions 4, with fewer reporting at sessions 8, 12, and 16. A lower percentage of women with revised fat gram goals are reporting scores compared to women with the original fat gram goals. The average fat score at Session 4 was 28.0, Session 8 was 24.4, at Session 12 was 23, and at Session 16 was 23.1. These self-reports compare favorably with the results from all Intervention women (Table 6.2), showing a reduction ranging from 1.7 to 3.9 grams of fat (Session 4, 16).

Table 6.4 - Intervention Program Maintenance Summary describes the performance of DM Intervention women at the Year 2 and 3 quarterly maintenance sessions, which start Year 2 of the Intervention program. Attendance and completion and percentage fat scores reported are lower in Summer than other seasons. Peer group activities are optional, though encouraged, when Maintenance starts in Year 2. Peer-led groups are a way to supplement the required nutritionist-led maintenance sessions with the intent of increased participant self-management and motivation. On average, 3.7% of women per month have had a peer group contact of those who have progressed beyond Year 1 Intervention (data not shown). This low number is likely due to staff workload impeding initiation and oversight of peer groups. Increasing peer group contacts is a goal of the Lead Nutritionists and CCC and a discussion topic on regional Lead Nutritionist calls.

6.3 Comparison of Dietary Intake

Dietary intake in DM is assessed at baseline and post-randomization in both the Intervention and Control arms with three instruments: the FFQ, the 4DFR, and the 24 Hour Recall (24 HR). Supplement intake is reported herein from Current Supplement information, which is obtained at selected time points in conjunction with current medications. All women in the DM complete an FFQ during screening (baseline) and at their first annual clinic visit. All other dietary assessments are administered on subsamples of participants.

Table 6.5 - Nutrient Intake Monitoring displays baseline, year one, and year two data by treatment arm for percent energy from fat, total energy, total fat, and saturated fat for DM studywide. *Table 6.6 - Nutrient Intake Monitoring among Minority Women* provides a parallel summary for minorities (all races and ethnicities combined). *Table 6.7 - Nutrient Intake Monitoring in Obese Women* provides a parallel summary for obese women (BMI>32.3 kg/m^2). *Table 6.8 - Nutrient Intake in Women Age 70-79* provides a parallel summary for women aged 70-79. *Table 6.9 - Nutrient Intake Monitoring for Women with Revised Fat Gram Goals* provides baseline and year one nutrient data for % energy from fat, total energy, total fat, and saturated fat for women who have received revised (lower) fat gram goals. Arithmetic means and standard deviations are presented for all nutrients.

Non-normally distributed data (total fat and saturated fat) were transformed logarithmically before testing for treatment differences by t-test.

Percent energy from fat at Year 1 among DM Intervention women, measured by the FFQ, is 24.4% on average, higher than the DM Intervention design assumption of 21.7% fat. Percent energy from fat at Year 1, measured by the 4DFR, is 21.7%. One can speculate that the differences between the FFQ and 4DFR (and between the FFQ and 24HR) are due to intrinsic differences in how data are collected by each of the instruments, an observation that is common to food reporting methodology. Other reasons for the discrepancy might be due to a cohort effect within the 4DFR sample population or that FFQ data are list-based estimates of food intake whereas 4DFR and 24HR data are reflective of actual food eaten. The post-Baseline 24HR data are collected six months after randomization and thus reflect early intervention effects of the DM. Percent energy from fat, studywide, in the Intervention group (21.0%) is significantly lower than in the Control group (31.8%) as measured in the 24HR (*Table 6.5*). Year 1 24HR are too few (21) to report.

FFQ data for year 2 are now available, although the sample size is relatively small (n=356 Intervention, n=545 Control). Fat intake (% energy) in the Intervention Group increased 1% and decreased <1% in the Control Group, on average, compared to year one.

The differences between treatment arms at years one and two are less than desirable, owing largely to the lower reported fat intake in the Controls and potentially to the Intervention group not achieving the design goals. Note that the baseline FFQ percentage of calories from fat averages are inflated, probably by about 3-4%, due to the use of the FFQ as a screening tool.

Tables 6.6, 6.7, and *6.8* report nutrient intake data from subgroups of DM women (minority, obese, aged 70-79). The three subgroups were selected due to potential risk of not adhering to the intervention or where little background data are available in the literature. A few general comments are offered about these data. In general, percent fat intake (FFQ) at Years 1 and 2 DM Intervention is higher among minority women than studywide. Nothing is notable about the data from obese women. Scientifically, a concern about obese women is underreporting of fat intake. We cannot interpret these data to refute or support this concern as there is not a way to truly measure fat intake. Regarding women aged 70-79, their mean fat intake is similar to studywide fat intake.

Thirty-one percent of DM Intervention women, studywide, had less than or equal to 20% energy from fat at Year 1 as measured by the FFQ (*Table 6.5*), yet 75% of DM Intervention women, studywide, met their fat gram goal at session 12, as assessed by self-monitoring (data not shown). We attribute this discrepancy in part to incomplete recording and in part to an apparent underestimation of fat intake by the self-monitoring process. Although 75% of women reported fat scores ≤ goal, only 84% of women recorded scores. This incomplete recording of scores may lead to a selection bias and overestimation of percentage of women who meet their fat goal. The self-monitoring process underestimation is likely due to a variety of factors, such as limitations of the self-monitoring instruments (by not having all-inclusive lists of foods) and recording bias. This apparent underestimation of fat intake by self-monitoring provided the basis for a decision to change the fat gram goal algorithm used for self-monitoring (implemented Sept. 15, 1996). The DM Intervention goal remains 20% energy from fat but the self-monitoring tool goals are adjusted

downward to approximately 15% of estimated post dietary change energy to account for this bias (most individual goals are now in the range 24-26 grams of fat daily).

Table 6.9 reports data from women who have a revised (lower) fat gram goal, were randomized after 6/15/95, and had the first annual visit on or before 9/1/96. There is a 12% difference in % energy from fat (FFQ) between Control and Intervention at Annual Visit 1 in these women compared to an 11% difference for women with the original fat gram goals compared to their Controls. With relatively little data yet, and no data to temporally compare original fat gram goals with revised fat gram goals, it is early to draw conclusions about the effectiveness of the revised fat gram goals towards meeting DM design assumptions though the observed value is in the range we had hoped to see. Although some women with revised fat gram goals were randomized before 6/15/96, we selected a randomization date of 6/15/95 for this analysis to provide a comparison group who had not been waiting an unusually long time from randomization to the beginning of intervention.

Table 6.10 - Body Weight displays baseline and year one body weight data per treatment arm for DM participants studywide, and for minority and obese participants and those aged 70-79. Modest weight loss would be consistent with adhering to a low-fat dietary pattern as the average intervention energy intake usually does not reach the pre-intervention level. Body weight, on average studywide, decreased 2.7 kg in the Intervention group and decreased 0.8 kg in the Control group one year after randomization. The difference between arms at year 1 is statistically significant ($p \leq 0.05$) for all participants, obese participants, and participants aged 70-79. The difference between arms at Year 1 is not statistically significant for minority women.

Table 6.11 - Selected Percentiles for Key Nutrients Based on FFQ Data from AV-1 and *Table 6.12 - Selected Percentiles for Key Nutrients Based on FFQ Data from AV-1 for Women with Revised Fat Gram Goals* present estimates of the upper and lower tails of the frequency distribution for reported intake of selected nutrients: % energy from fat; total energy; total fat; saturated fat; and calcium from dietary and total sources. These are intended to assist in evaluating participant safety, particularly the effect of the dietary intervention on nutrient intakes compared to the control group.

Total energy intake appears to be similar in the Intervention and Control groups studywide for the lower 5th and 10th percentiles, though both are lower than is nutritionally optimal for weight-maintaining women in the WHI age range. Percent energy from fat intake appears to be adequate for women in the DM Intervention even at the lower end of the frequency distribution (based on the 1993 FAO recommendations of a minimum of 15% energy from fat for adults). Assuming that polyunsaturated fat accounts for at least one-third of the total fat intake, we can extrapolate that essential fatty acid consumption is probably adequate.

Calcium intake, from both dietary and supplement sources, does not appear to be adversely impacted by the DM Intervention. If anything, calcium intake is slightly higher in DM Intervention women than Control women. Women at the lower ends of the frequency distribution in either the Control or Intervention groups are not meeting the RDA for calcium. (Calcium intake from antacids is assumed to be one dosage per day.)

Table 6.2

Intervention Program Adherence Summary

	Intervention Session			
	4	**8**	**12**	**16**
Participants Assigned	7461	7071	5589	4341
Attendance	85%	78%	70%	68%
Completion	98%	95%	91%	88%
Self-Monitoring				
Fat gram				
Score obtained	93%	88%	84%	80%
Average score	29.7	26.6	26.2	27.0
Average goal	28.5	28.7	29.9	31.2
Fruit/Vegetable				
Score obtained	n.a	85%	84%	80%
Average score	n.a	5.5	5.6	5.6
Grain				
Score obtained	n.a	85%	84%	80%
Average score	n.a	4.9	5.2	5.4

Table 6.3

Intervention Program Adherence Summary

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

	Intervention Session			
	4	**8**	**12**	**16**
Participants Assigned	3809	3437	2006	818
Attendance	84%	75%	67%	64%
Completion	97%	93%	86%	79%
Self-Monitoring				
Fat gram				
Score obtained	91%	84%	79%	68%
Average score	28.0	24.4	23.2	23.1
Average goal	24.7	24.7	24.8	24.9
Fruit/Vegetable				
Score obtained	n.a.	82%	79%	68%
Average score	n.a.	5.6	5.7	5.9
Grain				
Score obtained	n.a.	82%	78%	68%
Average score	n.a.	5.0	5.2	5.3

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

Table 6.4

Intervention Program Maintenance Summary

	Maintenance Session - Year 2[1]			
	Spring	**Summer**	**Fall**	**Winter**
Participants Assigned	2212	2710	1082	1578
Attendance	66%	62%	68%	64%
Completion	83%	77%	89%	85%
Self-Monitoring				
Fat gram				
Score obtained	71%	64%	78%	74%
Average score	27.1	27.0	26.7	28.1
Average goal	32.1	32.2	31.1	31.7
Fruit/Vegetable				
Score obtained	71%	64%	78%	74%
Average score	5.9	6.0	6.0	6.1
Goal				
Grain				
Score obtained	71%	64%	78%	74%
Average score	5.7	5.6	5.4	5.7
Goal				

[1] VCC only

Table 6.4 (continued)

Intervention Program Maintenance Summary

	Maintenance Session - Year 3[1]			
	Spring	**Summer**	**Fall**	**Winter**
Participants Assigned	<100 (data not shown)	337	<100 (data not shown)	<100 (data not shown)
Attendance	–	58%	–	–
Completion	–	64%	–	–
Self-Monitoring	–			
Fat Gram				
Score obtained	–	52%	–	–
Average score	–	27.0	–	–
Average goal	–	30.6	–	–
Fruit/Vegetable	–	52%	–	–
Score obtained	–	6.2	–	–
Goal	–	5.0	–	–
Grain				
Score obtained	–	52%	–	–
Average Score	–	5.6	–	–
Goal	–	6	–	–

[1] VCC only

Table 6.5

Nutrient Intake Monitoring

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
% Energy from Fat									
FFQ Baseline	9867	38.8	5.0	14769	38.9	5.0	0.1	0.1	0.29
FFQ Year 1[3]	4040	24.4	7.3	5882	35.5	7.1	11.0	0.1	0.00
FFQ Year 2[4]	356	25.5	7.6	545	34.9	7.0	9.3	0.5	0.00
4DFR Baseline	380	33.6	6.3	626	33.2	6.4	0.3	0.4	0.41
4DFR Year 1	172	21.7	6.8	277	32.5	6.4	10.8	0.6	0.00
24 Hr Recall, post-Baseline	73	21.0	9.1	105	31.8	7.2	10.8	1.2	0.00
24 Hr Recall Year 1	21	21.3	6.2	35	33.0	9.7	11.7	2.4	0.00
Total Energy (kcal)									
FFQ Baseline	9867	1812	727	14769	1801	711	11	9	0.32
FFQ Year 1	4040	1495	530	5882	1576	629	80	12	0.00
FFQ Year 2	356	1546	524	545	1603	593	57	39	0.00
4DFR Baseline	380	1751	456	626	1744	445	7	29	0.85
4DFR Year 1	172	1465	331	277	1637	449	172	40	0.00
24 Hr Recall, post-Baseline	73	1557	385	105	1685	499	128	69	0.14
24 Hr Recall, Year 1	21	1493	378	35	1505	457	13	118	0.92
Total Fat (g)									
FFQ Baseline	9867	78.9	36.0	14769	78.5	35.1	0.4	0.5	0.57
FFQ Year 1	4040	40.8	21.0	5882	63.1	30.9	22.2	0.6	0.00
FFQ Year 2	356	43.7	19.6	545	63.4	30.0	19.7	1.8	0.00
4DFR Baseline	380	66.1	24.7	626	65.3	23.6	0.8	1.6	0.53
4DFR Year 1	172	34.9	13.0	277	60.0	22.5	25.1	1.9	0.00
24 Hr Recall, post-Baseline	73	37.9	22.4	105	60.6	24.6	22.7	3.6	0.00
24 Hr Recall, Year 1	21	35.8	15.6	35	57.3	27.9	21.5	6.6	0.01
Saturated Fat (g)									
FFQ Baseline	9867	27.9	13.8	14769	27.6	13.4	0.2	0.2	0.28
FFQ Year 1	4040	14.2	7.9	5882	22.3	11.8	8.1	0.2	0.00
FFQ Year 2	356	15.1	7.2	545	22.4	11.5	7.3	0.7	0.00
4DFR Baseline	380	22.0	9.3	626	21.5	8.8	0.5	0.6	0.38
4DFR Year 1	172	11.0	4.8	277	20.1	8.5	9.1	0.7	0.00
24 Hr Recall, post-Baseline	73	12.2	7.6	105	19.8	8.9	7.6	1.3	0.00
24 Hr Recall, Year 1	21	11.8	7.1	35	18.6	9.9	6.8	2.5	0.01

[1] Absolute difference

[2] P-values are based on testing in the natural log scale except for % Energy from Fat.

[3] 1245 (31%) Intervention women had ≤ 20% energy from fat at year 1.

[4] 84 (24%) Intervention women had ≤ 20% energy from fat at year 2.

Table 6.6

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	1714	39.4	5.2	2550	39.6	5.1	0.2	0.2	0.29
FFQ Year 1[3]	526	27.1	8.1	731	35.9	7.5	8.8	0.4	0.00
FFQ Year 2[4]	32	29.4	8.7	41	34.1	6.9	4.8	1.8	0.01
4DFR Baseline	138	33.7	6.3	238	34.0	6.3	0.3	0.7	0.67
4DFR Year 1	16	24.0	6.3	41	32.9	7.0	8.9	2.0	0.00
24 Hr Recall post-Baseline	8	25.0	8.7	14	32.9	7.3	7.8	3.5	0.04
Total Energy (kcal)									
FFQ Baseline	1714	1765	818	2550	1758	825	7	26	0.70
FFQ Year 1	526	1426	577	731	1439	713	13	38	0.43
FFQ Year 2	32	1552	563	41	1482	666	71	147	0.84
4DFR Baseline	138	1704	459	238	1732	450	27	48	0.49
4DFR Year 1	16	1350	303	41	1507	480	157	129	0.40
24 Hr Recall post-Baseline	8	1213	352	14	1627	448	414	185	0.06
Total Fat (g)									
FFQ Baseline	1714	77.9	39.8	2550	78.0	40.7	0.1	1.3	0.97
FFQ Year 1	526	43.4	24.4	731	58.7	34.8	15.3	1.8	0.00
FFQ Year 2	32	50.6	23.1	41	57.2	29.4	6.6	6.3	0.42
4DFR Baseline	138	64.3	22.8	238	66.2	24.1	2.0	2.5	0.48
4DFR Year 1	16	35.7	10.7	41	56.8	23.5	21.1	6.1	0.01
24 Hr Recall post-Baseline	8	32.5	10.5	14	58.8	18.9	26.3	7.3	0.00
Saturated Fat (g)									
FFQ Baseline	1714	26.2	14.2	2550	26.2	14.9	0.1	0.5	0.87
FFQ Year 1	526	14.6	8.8	731	19.7	12.6	5.1	0.6	0.00
FFQ Year 2	32	16.6	7.6	41	19.8	11.2	3.2	2.3	0.32
4DFR Baseline	138	20.6	8.4	238	21.2	8.7	0.6	0.9	0.56
4DFR Year 1	16	10.8	3.8	41	18.3	8.4	7.5	2.2	0.00
24 Hr Recall post-Baseline	8	9.9	4.0	14	20.3	7.7	10.4	2.9	0.00

[1] Absolute difference

[2] P-values are based on testing in the natural log scale except for % Energy from Fat.

[3] 102 (19%) Minority Intervention women had ≤ 20% energy from fat at year 1.

[4] 4 (12%) Minority Intervention women had ≤ 20% energy from fat at year 2.

Table 6.7

Nutrient Intake Monitoring in Obese[1] Women

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[2]	SE	p-value[3]
% Energy from Fat									
FFQ Baseline	2438	39.8	5.4	3665	39.8	5.3	0.0	0.1	0.74
FFQ Year 1[4]	934	25.3	7.9	1327	36.0	7.6	10.7	0.3	0.00
FFQ Year 2[5]	75	26.2	7.6	116	35.0	7.4	8.9	1.1	0.00
4DFR Baseline	380	33.6	6.3	626	33.2	6.4	0.3	0.4	0.41
4DFR Year 1	172	21.7	6.8	277	32.5	6.4	10.8	0.6	0.00
24 Hr Recall post-Baseline	18	24.6	12.0	22	34.8	5.1	10.2	2.8	0.00
Total Energy (kcal)									
FFQ Baseline	2438	1978	833	3665	1929	777	49	21	0.04
FFQ Year 1	934	1550	589	1327	1651	708	100	28	0.01
FFQ Year 2	75	1550	550	116	1537	606	13	87	0.09
4DFR Baseline	380	1751	456	626	1744	445	7	29	0.85
4DFR Year 1	172	1465	331	277	1637	449	172	40	0.00
24 Hr Recall	18	1401	404	22	1707	510	305	148	0.06
Total Fat (g)									
FFQ Baseline	2438	88.3	42.5	3665	86.0	39.1	2.3	1.1	0.07
FFQ Year 1	934	44.1	24.8	1327	67.1	34.9	23.0	1.3	0.00
FFQ Year 2	75	45.4	21.9	116	61.5	31.3	16.1	4.1	0.00
4DFR Baseline	380	66.1	24.7	626	65.3	23.6	0.8	1.6	0.53
4DFR Year 1	172	34.9	13.0	277	60.0	22.5	25.1	1.9	0.00
24 Hr Recall post-Baseline	18	40.6	28.6	22	65.7	20.7	25.1	7.8	0.00
Saturated Fat (g)									
FFQ Baseline	2438	31.2	16.1	3665	30.5	14.9	0.7	0.4	0.12
FFQ Year 1	934	15.3	9.0	1327	23.8	13.2	8.5	0.5	0.00
FFQ Year 2	75	15.7	7.9	116	21.6	11.5	5.9	1.5	0.00
4DFR Baseline	380	22.0	9.3	626	21.5	8.8	0.5	0.6	0.38
4DFR Year 1	172	11.0	4.8	277	20.1	8.5	9.1	0.7	0.00
24 Hr Recall post-Baseline	18	12.5	10.2	22	22.5	7.4	10.0	2.8	0.00

[1] Obesity defined as BMI > 32.3 kg/m^2.

[2] Absolute difference

[3] P-values are based on testing in the natural log scale except for % Energy from Fat.

[4] 263 (28%) Obese Intervention women had ≤ 20% energy from fat at year 1.

[5] 15 (20%) Obese Intervention women had ≤ 20% energy from fat at year 2.

Table 6.8

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	1350	38.5	4.6	2017	38.4	4.7	0.1	0.2	0.48
FFQ Year 1[3]	541	25.4	7.1	806	35.5	6.6	10.1	0.4	0.00
FFQ Year 2[4]	45	27.8	8.6	62	36.0	6.4	8.2	1.5	0.00
4DFR Baseline	48	31.6	5.6	74	33.6	6.4	2.0	1.1	0.07
4DFR Year 1	22	22.1	4.9	39	33.8	5.8	11.7	1.5	0.00
24 Hr Recall post-Baseline	12	20.3	9.3	11	30.8	5.9	10.5	3.3	0.00
Total Energy (kcal)									
FFQ Baseline	1350	1688	656	2017	1681	676	8	23	0.53
FFQ Year 1	541	1433	547	806	1536	634	103	33	0.02
FFQ Year 2	45	1499	552	62	1511	550	12	108	0.38
4DFR Baseline	48	1559	358	74	1614	390	55	70	0.45
4DFR Year 1	22	1351	294	39	1522	395	170	97	0.12
24 Hr Recall post-Baseline	12	1644	394	11	1743	443	99	175	0.59
Total Fat (g)									
FFQ Baseline	1350	72.7	31.5	2017	72.1	32.2	0.7	1.1	0.42
FFQ Year 1	541	40.8	22.2	806	61.4	30.2	20.5	1.5	0.00
FFQ Year 2	45	45.4	19.2	62	61.1	26.0	15.7	4.6	0.00
4DFR Baseline	48	55.6	18.7	74	61.4	21.9	5.9	3.8	0.17
4DFR Year 1	22	32.9	9.1	39	57.7	19.1	24.8	4.3	0.00
24 Hr Recall post-Baseline	12	40.1	26.2	11	60.1	22.8	20.0	10.3	0.02
Saturated Fat (g)									
FFQ Baseline	1350	25.7	12.1	2017	25.3	12.4	0.4	0.4	0.20
FFQ Year 1	541	14.4	8.3	806	21.7	11.6	7.4	0.6	0.00
FFQ Year 2	45	15.7	7.2	62	21.2	9.8	5.6	1.7	0.00
4DFR Baseline	48	18.7	7.2	74	20.5	8.7	1.8	1.5	0.32
4DFR Year 1	22	10.5	4.3	39	19.9	7.3	9.4	1.7	0.00
24 Hr Recall post-Baseline	12	11.8	7.2	11	20.4	10.4	8.6	3.7	0.01

[1] Absolute difference

[2] P-values are based on testing in the natural log scale except for % Energy from Fat.

[3] 134 (25%) Intervention women aged 70-79 had ≤ 20% energy from fat at year 1.

[4] 7 (16%) Intervention women aged 70-79 had ≤ 20% energy from fat at year 2.

Table 6.9

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	5861	38.8	5.0	9250	38.8	4.9	0.02	0.1	0.84
FFQ Year 1	440	24.1	7.4	984	36.1	6.9	12.0	0.4	0.00
Total Energy (kcal)									
FFQ Baseline	5861	1802	705	9250	1800	711	2	12	0.69
FFQ Year 1	440	1456	474	984	1599	644	143	34	0.00
Total Fat (g)									
FFQ Baseline	5861	78.3	34.7	9250	78.2	35.0	0.1	0.6	0.70
FFQ Year 1	440	39.1	19.8	984	65.0	32.3	25.9	1.7	0.00
Saturated Fat (g)									
FFQ Baseline	5861	27.7	13.3	9250	27.6	13.5	0.1	0.2	0.44
FFQ Year 1	440	13.4	7.5	984	22.8	12.5	9.5	0.6	0.00

[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 are based on testing in the natural log scale except for % Energy from Fat.

Table 6.10
Body Weight

	Intervention			Control			Difference		
Body Weight (kg)	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	**Mean[1]**	**SE**	**p-value[2]**
All Participants									
Baseline	9867	76.5	16.1	14769	76.2	15.9	0.3	0.2	0.17
Year 1	4093	73.8	16.5	5981	75.4	16.0	1.7	0.3	0.00
Year 2	1200	74.1	16.6	1791	75.2	16.1	1.0	0.6	0.10
Minority Participants									
Baseline	1714	80.3	18.0	2550	79.6	18.2	0.6	0.6	0.25
Year 1	542	79.7	19.5	773	79.3	18.1	0.4	1.0	0.69
Year 2	119	79.5	18.8	171	77.4	16.4	2.1	2.1	0.30
Obese Participants[3]									
Baseline	2438	96.8	14.1	3665	96.2	13.8	0.7	0.4	0.06
Year 1	949	92.9	14.8	1358	94.1	12.8	1.2	0.6	0.05
Year 2	255	92.9	13.3	373	92.6	13.0	0.2	1.1	0.82
Participants Aged 70-79									
Baseline	1350	72.1	13.8	2017	72.1	13.7	0.0	0.5	1.00
Year 1	551	69.4	13.9	825	72.0	14.8	2.6	0.8	0.00
Year 2	141	70.2	15.7	223	71.5	14.7	1.3	1.6	0.42

[1] Absolute difference

[2] P-values are based on testing in the natural log scale except for % Energy from Fat.

[3] Obesity defined as BMI > 32.2 kg/m^2.

Table 6.11

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

Intervention	5%	10%	50%	90%	95%
% Energy from Fat	14.4	15.9	23.5	34.2	38.2
Total Energy (kcal)	747	891	1446	2136	2390
Total Fat (g)	16.5	19.8	36.8	65.8	78.6
Saturated Fat (g)	5.3	6.5	12.6	23.5	28.0
Calcium FFQ (mg)	272	345	700	1356	1571
Total Calcium (mg)	282	366	812	1730	2138
Control					
% Energy from Fat	23.4	26.4	35.6	44.3	47.1
Total Energy (kcal)	725	862	1493	2369	2703
Total Fat (g)	23.8	29.7	57.7	101.9	119.0
Saturated Fat (g)	7.8	9.8	20.2	37.3	43.9
Calcium FFQ (mg)	235	300	627	1219	1427
Total Calcium (mg)	250	321	718	1595	1928

Table 6.12

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

Intervention[1]	5%	10%	50%	90%	95%
% Energy from Fat	14.7	15.5	22.8	34.0	38.4
Total Energy (kcal)	814	927	1432	2065	2309
Total Fat (g)	17.1	19.7	35.2	60.2	75.6
Saturated Fat (g)	5.4	6.3	11.7	21.5	26.3
Calcium FFQ (mg)	273	344	717	1343	1496
Total Calcium (mg)	278	374	828	1723	1973
Control[2]					
% Energy from Fat	24.2	27.2	36.1	44.9	47.1
Total Energy (kcal)	757	899	1507	2405	2771
Total Fat (g)	26.0	31.1	59.6	106.0	121.3
Saturated Fat (g)	8.4	10.5	20.3	37.6	45.6
Calcium FFQ (mg)	250	305	640	1255	1471
Total Calcium (mg)	268	321	764	1634	1915

[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.

7. CaD Intervention Status

7.1 Adherence to Supplements

Adherence to CaD study supplements is determined using the same procedures and definitions as HRT. See *Section 5.1 - Adherence to Medications* for details.

Table 7.1 - CaD Adherence Summary presents the current experience among all CaD participants who have had at least one follow-up visit for CaD. In calculating adherence among all CaD participants, women who are missing this adherence information are classified as non-adherent (consuming <80% of expected tablets). This provides an underestimate of adherence. Adherence is also shown among all women who have provided an adherence measure. This is likely to over-estimate adherence somewhat. Thus, at SAV-2, the true value is likely to be between 46% and 58%. Age, ethnicity and income are emerging as predictors of adherence with younger and minority women having lower adherence. Interestingly, lower income women have better adherence rates than upper income women. Education may also be a factor as some of the initial estimates show large but non-significant effects. CaD participants who are also participants in HRT are more adherent than DM only women. This is likely associated more with pill-taking behavior than with any interaction between the interventions. More importantly, even the most optimistic estimate is much lower than anticipated, requiring corrective action.

Table 7.2 - CaD Drop-out Rate Summary provides a display of participants who have reported stopping the CaD intervention at any time post-randomization broken down by the same risk factors. A drop-out rate of 6% after one year (at AV-2) was assumed in the design. With an average of 7 months of follow-up, the current estimate is 7.9%. Assuming a constant drop-out rate, we would project an annual rate of 13.4%, well beyond the design value.

There is a noteworthy range among clinics in the proportion of women who are considered active in the study and are due for resupply of their supplements but have not received them (range is 1% to 34%). This variability is affected by tracking problems, delays in reporting drop-outs, or dose reductions.

The CaD Advisory Committee has discussed the adherence problems and recommended several approaches that are under development, including: asking for additional changes in the tablet formulation; adding a 4 week post-randomization phone contact to assess and encourage adherence; and incorporating a taste-test during screening. Some information on the effect of these efforts should be available for our next semi-annual report.

Table 7.1
CaD Adherence Summary

	All CaD Participants[1]		Participants with Counts[1]	
	N	% Adherent[2]	N	% Adherent
SAV-2	3169	46.1	2505	58.3
Age				
50-54	664	39.6***	506	52.0***
55-59	732	43.0	567	55.6
60-69	1332	49.5	1081	61.1
70-79	441	50.3	351	63.2
Ethnicity				
Minority	379	35.1***	277	48.0***
White	2788	47.6	2227	59.6
Education				
0-8 Years	40	47.5	29	65.5
Some H.S. or diploma	731	47.7	595	58.7
Any school after H.S.	2390	45.5	1874	58.1
Income				
< $10,000	117	53.8**	101	62.4
$10,000-$19,999	388	49.5	319	60.2
$20,000-$34,999	859	47.8	692	59.4
$35,000-$49,999	655	45.8	520	57.7
$50,000-$74,999	591	45.2	472	56.6
$75,000-$99,999	233	45.5	174	60.9
$100,000-$149,999	136	33.1	89	50.6
$150,000 or more	63	28.6	43	41.9
HRT				
Yes	1223	56.0***	1092	62.7***
Hysterectomy	499	53.7	438	61.2
No Hysterectomy	724	57.6	654	63.8
No	1946	39.8	1413	54.8
DM				
Yes	2465	43.4***	1872	57.2
Intervention	973	43.4	743	56.8
Control	1492	43.5	1129	57.5
No	704	55.3	633	61.5
HRT/DM	519	57.0	459	64.5

[1] Includes participants that have stopped intervention/meds.
[2] If no collection then considered < 80% adherent.
* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

Table 7.1 (continued)
CaD Adherence Summary

	All CaD Participants[1]		Participants with Counts[1]	
	N	% Adherent[2]	N	% Adherent
AV-2	826	41.0	601	56.4
Age				
50-54	189	39.2	135	54.8
55-59	228	38.2	172	50.6
60-69	324	42.9	235	59.1
70-79	85	45.9	59	66.1
Ethnicity				
Minority	75	30.7	48	47.9
White	751	42.1	553	57.1
Education				
0-8 Years	7	14.3	5	20.0
Some H.S. or diploma	196	45.4	146	61.0
Any school after H.S.	620	40.0	449	55.2
Income				
< $10,000	27	44.4	19	63.2
$10,000-$19,999	99	48.5	75	64.0
$20,000-$34,999	199	43.7	151	57.6
$35,000-$49,999	179	40.2	130	55.4
$50,000-$74,999	153	43.8	112	59.8
$75,000-$99,999	71	35.2	53	47.2
$100,000-$149,999	44	25.0	30	36.7
$150,000 or more	18	22.2	11	36.4
HRT				
Yes	266	54.1***	210	68.6***
Hysterectomy	111	45.0*	81	61.7
No Hysterectomy	155	60.6	129	72.9
No	560	34.8	391	49.9
DM				
Yes	694	39.2*	503	54.1**
Intervention	268	41.0	190	57.9
Control	426	38.0	313	51.8
No	132	50.8	98	68.4
HRT/DM	134	57.5	112	68.8

[1] Includes participants that have stopped intervention/meds.
[2] If no collection then considered < 80% adherent.
* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

Table 7.2
CaD Drop-out Rate Summary

	Number Randomized[1]	% Inactive
Overall	7390	7.9
Age		
50-54	1507	8.2
55-59	1863	7.8
60-69	3011	7.5
70-79	1009	8.7
Ethnicity		
Minority	922	7.6
White	6461	7.9
Education		
0-8 Years	108	7.4
Some H.S. or diploma	1635	6.9
Any school after H.S.	5621	8.2
Income		
< $10,000	263	6.5
$10,000-$19,999	839	7.2
$20,000-$34,999	1915	7.6
$35,000-$49,999	1559	7.6
$50,000-$74,999	1401	7.5
$75,000-$99,999	615	8.6
$100,000-$149,999	348	8.9
$150,000 or more	128	14.8
HRT		
Yes	2861	5.2
Hysterectomy	1142	7.6
No Hysterectomy	1719	3.7
No	4529	9.5
DM		
Yes	5647	8.8
Intervention	2201	10.6
Control	3446	7.7
No	1743	4.8
HRT/DM	1118	5.9

[1] Average follow-up time is approximately 7 months.

8. Outcomes

8.1 Overview

The identification of potential WHI outcomes for CT participants begins with the self-administered Form 33 - Medical History Update, which is to be completed every six months. The Clinical Centers then follow up on these self-reported outcomes by obtaining medical records and submitting them for review by a local physician adjudicator. A portion of the locally adjudicated outcomes are then reviewed centrally in an attempt to standardize the definition of WHI outcomes study wide.

Over the past six months, the development of the outcomes investigation process has continued to advance. This report of the experience of the WHI with respect to protocol defined outcomes includes data on the following items:

1. Timeliness of Outcome Reporting Process
2. Self-reported Outcomes
3. Preliminary Reports of Deaths and Serious Adverse Experiences
4. Verified Outcomes

8.2 Timeliness of Outcome Reporting Process

At the June, 1996 meeting of the Data Safety Monitoring Board for WHI, DSMB members had questions regarding the length of time required for the various steps of the outcome verification process. Current estimates based on the WHI experience to date are presented below. When appropriate, estimates are presented based on the cumulative data collected since the inception of WHI, as well as on only the most recently collected outcomes data.

8.2.1 Completion of Form 33 by CT participants

This form is used to collect self reported data pertaining to potential WHI outcomes. Participants on any part of the CT are to complete a Form 33 every 6 months. The following table provides the percentage of participants' forms which are collected from the participants and received by the appropriate CC within the designated time periods following the date the Form 33 was due per protocol. From this table it can be seen that a little over 80% of Form 33s are received at the CCs within 30 days of the due date, and nearly 90% are received within 60 days of the due date.

	≤ 30 d	≤ 60 d	≤ 90 d	≤ 180 d
Cumulative	83%	89%	91%	93%
Due after May 1, 1996	81%	87%	89%	

8.2.2 Completion of Form 33D by those participants with potential primary outcomes

Under the revised outcomes collection procedures, Form 33 is used to collect those outcomes that are never investigated further and to screen for the need to collect more detailed information on the more important WHI outcomes. Participants who indicate on Form 33 that they have had hospitalizations or recent cancer or fracture diagnoses are then asked to complete a Form 33D. The following table provides the percentage of participants' forms which are collected from the participants and received by the appropriate CC within the designated time periods following the

receipt of the Form 33. Because Form 33D was introduced in March, 1996, all estimates are based on recent data. From this table it can be seen that approximately one-third of Form 33Ds have not been received two months after the Form 33 was processed.

	< 30 d	< 60 d	< 80 d
Since March 15, 1996	58%	66%	69%

8.2.3 WHILMA analysis of Form 33D for potential outcomes needing investigation

Following collection of the detailed information regarding potential WHI outcomes on Form 33D, the CCs are to process the forms within WHILMA to identify those outcomes requiring collection of medical records and adjudication of outcomes. The following table provides the percentage of participants' forms which have been analyzed by WHILMA within the designated time periods following the receipt of the Form 33D. Although WHILMA was also required for Form 33s under the initial outcomes collection process, that processing was not implemented until 1996. Hence, the estimates presented below do not include the processing of those early forms.

	< 30 d	< 60 d	< 80 d
Since June 1, 1996	64%	83%	93%

8.2.4 Collection of medical documentation

After WHILMA has identified those potential outcomes requiring detailed investigation, the CCs are to obtain specific medical records from the health care providers as indicated by WHILMA (and the WHI manuals). It is difficult to obtain reliable estimates of the time required for this process from the early procedures for outcomes documentation. Hence, until the outcomes process is dealing only with data collected using Form 33D, the distribution of completion times for these tasks will need to be inferred from the completion times for the entire adjudication process given in item 8.2.6 below.

8.2.5 Local adjudication

When all medical documentation has been obtained for a particular adjudication case, that documentation is to be forwarded to a local physician adjudicator at the CC. The following table provides the percentage of adjudication cases which have been returned by the local adjudicator within the designated time periods measured from the time of receipt of all medical records at the CC.

	< 30 d	< 60 d	< 80 d
Cumulative	52%	60%	62%
Since June 1, 1996	70%	74%	75%

8.2.6 Adjudication Process from Form 33 Due Date to Local Adjudication

The following table provides the percentage of Form 33s for which all identified potential WHI outcomes have been completely investigated within the designated time periods following the due date for the semi-annual Form 33s. From this table it can be seen that approximately 80% of outcomes investigations are completed within 60 days of the due date for the semi-annual Form 33s.

	≤ 30 d	≤ 60 d	≤ 80 d	≤ 120 d	≤ 180 d
Cumulative	75%	80%	81%	83%	84%
Since May 1, 1996	76%	82%	84%	85%	

It should be noted, however, that the preponderance of Form 33s reported as having complete investigations in the above table had no potential WHI outcomes reported. That is, at this early stage of the CT, most participants report no WHI outcomes on their Form 33s. When attention is restricted to those Form 33s requiring collection of more detailed information on a Form 33D, the percentage of those Form 33s having completed investigation of all identified potential WHI outcomes within the designated time period following the due date for receipt of the Form 33 by the CC is as presented in the following table. Thus, the outcomes process is completed fairly quickly for those participants not reporting potential WHI outcomes, but only about 25% of the outcomes investigations are completed in less than four months for participants reporting an overnight hospitalization or treatment of fractures or cancer.

	≤ 30 d	≤ 60 d	≤ 80 d	≤ 120 d
Since March 15, 1996	11%	17%	20%	23%

8.3 Self-Reported Outcomes

Due to the time involved in obtaining medical records and reviewing those records for WHI outcomes, there will tend to be a substantial delay between the ascertainment of a potential WHI outcome on a Form 33 and the final verification of that outcome. For this reason, monitoring reports will include counts of self-reported outcomes which are still pending verification.

When reviewing the results reported for the unverified self-reported outcomes, it is important to keep in mind the limitations of such data. In particular, although the participants are asked to report only those potential outcomes occurring since their last medical history update (Form 33), it is apparent that the subtleties behind such a request are missed by some women. These errors will be identified in the outcome verification process, however the results presented in this report will not yet have been corrected.

As of August 31, 1996, one or more Form 33's have been completed by 21,407 participants out of 32,406 participants randomized to date (many participants were randomized less than six months prior to the date of data analysis). The average length of follow up for those participants is 13.30 months (range 0.62 to 32.27 months).

Table 8.1 presents the counts and annualized proportion of patients reporting potential WHI outcomes for the HRT, DM and CaD clinical trials, respectively. For HRT these data are presented by hysterectomy status. Overall, approximately 13.1% of participants report at least one hospitalization since randomization, with similar distributions in both HRT and DM components. The incidences of specific cardiovascular, cancer, or fracture outcomes are also displayed in *Table 8.1*.

8.4 Preliminary Reports of Deaths and Serious Adverse Experiences

According to the WHI protocol, deaths of participants while on study are to be reported to the Clinical Coordinating Center within 48 hours. These deaths are then investigated and locally

adjudicated by a process similar to that for Form 33 data. Since the beginning of the clinical trial, the CCC has received reports of 69 deaths for CT participants, and the CT enrollment status for those participants is displayed in *Table 8.1*. Serious adverse experiences (SAEs) are reported to the CCC by the individual clinics. For the purposes of this report, all SAEs are reported with the WHI outcomes (e.g., cancer, stroke).

8.5 Verified WHI Outcomes

The CCs began data entering the results of local adjudication of the self-reported outcomes in December, 1995. As of August 31, 1996, a total of 435 WHI outcomes on 317 CT participants have been locally adjudicated and entered into the WHILMA data base. *Table 8.2* presents the number of locally verified WHI outcomes reported for participants on the HRT and DM clinical trials. It is still too early in the CaD component for local adjudication of self-reported outcomes to be complete for any events reported after CaD randomization. It should also be noted that the outcomes reported in *Table 8.2* continue to represent data from about half of the CCs. Over half of the locally adjudicate outcomes come from just six CCs, and a single CC (Buffalo) is the source for 17% of the locally adjudicated outcomes.

Owing to the sparseness of the locally adjudicated outcomes, there is not yet sufficient information to be able to analyze the reliability of the self reported outcomes. Furthermore, the first central review of the locally adjudicated outcomes will be taking place in November, 1996 for cardiovascular and mortality outcomes. Cancer and fracture central adjudication will similarly be starting during Fall, 1996.

In light of the above, the results of *Table 8.2* must be interpreted quite cautiously. It is not yet clear whether these locally adjudicated cases are at all representative of the CT participants as a whole.

Table 8.1

Counts (Annualized Percentages) of Participants with Self-Reported Outcomes

(Data Entered Through August 31, 1996)

	HRT		DM	CaD
	No Uterus	Intact Uterus		
Number of participants with *Form 33*[*]	3086	4579	16405	3345
Mean follow-up (months)[**]	13.2	13.0	13.5	7.1
Hospitalizations				
Ever	477 (14.0%)	564 (11.4%)	2170 (11.7%)	271 (13.6%)
Two or more	129 (3.8%)	171 (3.5%)	632 (3.4%)	48 (2.4%)
Cardiovascular Hospitalizations				
Angina	26 (0.8%)	27 (0.5%)	84 (0.5%)	20 (1.0%)
Heart Attack	18 (0.5%)	14 (0.3%)	29 (0.2%)	9 (0. 5%)
Heart Failure	4 (0.1%)	6 (0.1%)	16 (0.1%)	2 (0.1%)
CABG or PTCA	22 (0.6%)	22 (0.4%)	43 (0.2%)	14 (0.7%)
Carotid Endarterectomy	0 (0.0%)	4 (0.1%)	8 (0.0%)	1 (0.1%)
PVD	2 (0.1%)	3 (0.1%)	5 (0.0%)	0 (0.0%)
DVT	4 (0.1%)	13 (0.3%)	21 (0.1%)	2 (0.1%)
Pulmonary Embolism	0 (0.0%)	4 (0.1%)	13 (0.1%)	0 (0.0%)
Other CV hospitalization	37 (1.1%)	23 (0.5%)	135 (0.7%)	9 (0.5%)
Stroke	15 (0.4%)	15 (0.3%)	38 (0.2%)	3 (0.2%)
Cancer	68 (2.0%)	83 (1.7%)	364 (2.0%)	42 (2.1%)
Breast	6 (0.2%)	13 (0.3%)	61 (0.3%)	12 (0.6%)
Ovary	1 (0.0%)	1 (0.0%)	9 (0.0%)	0 (0.0%)
Endometrial	0 (0.0%)	2 (0.0%)	6 (0.0%)	0 (0.0%)
Colorectal	6 (0.2%)	9 (0.2%)	21 (0.1%)	3 (0.2%)
Other (non-skin)	7 (0.2%)	11 (0.2%)	49 (0.3%)	8 (0.4%)
Fractures	111 (3.3%)	147 (3.0%)	517 (2.8%)	57 (2.9%)
Hip	3 (0.1%)	2 (0.0%)	11 (0.1%)	2 (0.1%)
Hysterectomy	5 (0.1%)	26 (0.5%)	98 (0.5%)	13 (0.7%)
Diabetes (treated)	101 (3.0%)	93 (1.9%)	342 (1.8%)	49 (2.5%)
DEATHS	16	16	50	8

[*] Number of participants with at least one *Form 33 - Medical History Update* having valid data regarding hospitalizations.

[**] Mean follow-up is computed as the mean number of *Form 33's* per patient times 6 months.

Table 8.2

Counts of Participants with Locally Verified Outcomes for Hormone Replacement Therapy Component

(Data Entered through August 31, 1996)

	HRT		DM
	No Uterus	Intact Uterus	
Cardiovascular Hospitalizations			
Coronary Heart Disease			
Myocardial Infarction	6	2	11
Sudden coronary death	1	0	1
Other Cardiovascular Disease			
Angina	5	4	21
Congenital Heart Failure	2	1	9
Revascularization	6	1	11
Carotid	0	1	4
Peripheral Vascular Disease	0	0	1
Stroke	4	1	10
Deep Vein Thrombosis	1	3	2
Pulmonary Embolism	0	2	1
Cancer			
Major cancers			
Breast	1	4	21
Ovary	0	0	0
Endometrial	0	0	1
Colorectal	1	3	3
Other (non-skin)	4	6	14
Fractures	21	29	131
Hip	0	0	2
Hysterectomy	0	11	17
DEATHS	4	1	12

9. Clinical Center Performance Monitoring

9.1 Performance Monitoring Plan

In June 1995, the CCC implemented a four-step plan for monitoring and assisting CC performance. The purpose of the four steps is 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. As part of this four-step plan, the functions of the Regional Resource Center (RRC) at Bowman Gray School of Medicine were changed to include activities related to this new plan. The RRC was also renamed the Clinical Facilitation Center (CFC) to reflect this change in activities. The four monitoring levels are described below. Progress of the CC monitoring and follow-up is reported to the Steering Committee on a monthly basis.

Level 1: Routine Performance Monitoring and Follow-up

CCC quality assurance staff and lead staff liaisons regularly contact the clinic lead staff, review database reports, and perform standard QA visits to all clinics. They monitor clinic-specific and study-wide performance in key areas to provide timely and routine feedback on performance to the clinics in question and to provide assistance (e.g., advice, training) where performance needs improvement.

In July, the Council approved the QA Task Force recommendations for prioritizing and streamlining QA activities. In response to the recommendations, the content and frequency of the QA visits was streamlined. Beginning this fall, QA visits will be reduced from a 3-day to a 2-day visit for CCs without satellite sites and from 4 days to 3 days for CCs with satellite sites. To accommodate the shorter visits, the standard content of the visits is being reduced to allow time to focus on high priority areas and on CC-specific issues as needed. In addition, the frequency of the visits has been reduced from one per year to one every other year for CCs with good performance at the previous QA visit. As of June, 1996, all NCCs had had an initial QA visit and all VCCs have had a second annual visit.

Level 2: Performance Monitoring Committee

The Performance Monitoring Committee (PMC), formed in July 1995, reviews and notes persistent concerns in clinic performance. The Committee membership includes two members from the CFC, two members from the Project Office, and two members from the CCC. Other CCC, Project Office, and CFC scientists and staff regularly participant in the PMC calls and meetings. The PMC, meeting via regular conference calls, determines the assistance or other action that may be needed at selected clinics in the upcoming month. The PMC also identifies the person(s) who will, if asked, carry out such activities and identifies any study-wide issues to be brought to the attention of the Steering Committee

Level 3: Follow Up on Persistent Issues

The CFC is responsible for seeing that the recommended activities identified by the PMC are carried out in a timely fashion. The CFC staff conducts these interactions where appropriate or requests assistance of another person or group with specialized expertise in the area of concern. A Level 3 site visit may be conducted with one to three members from the CFC, Project Office and/or CCC, but without selected PIs or lead staff from the other clinics.

Level 4: Performance Enhancement Site Visit.

If the interactions with the PMC do not yield timely results, or if there are sufficiently serious clinic issues, a Level 4 performance enhancement site visit is conducted. In addition to CFC staff, the site visit team will typically include investigators and staff from other WHI clinics and a representative from the Project Office and the CCC. The composition of the site visit team depends, in great part, on the specific problem areas to be addressed. The CFC takes the lead in coordinating and arranging these visits, prepares a written report summarizing the site visit team's finding (for review by the site visit team), submits the report to the chair of the PMC, and monitors the progress toward achieving site visit recommendations. A copy of the final report is sent to the clinic, Project Office, and CCC.

9.2 PMC Summary Report

A PMC Summary Report was developed to assist the PMC in monitoring the clinic performance. The data summary tables include data on the following clinic activities: recruitment, recruitment of minorities for Pool 1 clinics, HRT, DM, and CaD follow-up and retention, HRT, DM, and CaD intervention, outcomes, subcontractor data, and data management. Within each table, the performance of each clinic is detailed for key activities related to the listed category. For example, the summary recruitment table shows the cumulative percent randomizations/enrollments into each study component and the percent of goal for the 70 - 79 age group. The tables also include a percent of goal over a previous time period to allow easy monitoring of trends within each clinic. The summary recruitment table includes percent of randomization/enrollment goal for the previous two quarters, and the other tables include cumulative percent through the previous quarter. Within each table, the final column shows a summary percentage for the activities presented in the table. Footnotes on each table indicate from which routine database reports the data come. Clinic performance is further summarized in one summary table listing the summary percentages of each of the previous tables, thereby presenting an overview of clinic performance in one table. The PMC report, showing cumulative data through August 31, 1996 is shown in *Table 9.1 - Clinical Center Performance Summary*. Possible additions to the report include a summary of the QA visits conducted by the CCC staff.

The entire PMC report is updated at the CCC every quarter and sent to the PMC. The recruitment summary table is updated monthly and used for the routine monitoring of specific CCs reviewed on the routine PMC calls. A copy of each quarterly PMC report is sent to each clinic PI, and an electronic copy is published to the CC fileservers.

9.3 PMC Committee Activity

The PMC began meeting via conference call on August 7, 1995. Current membership includes Anne McTiernan, chair of the PMC; Garnet Anderson and Andrea LaCroix, Co-Project Directors of the CCC; Ross Prentice, PI of CCC; Curt Furburg, PI of the CFC; Sally Shumaker, Co-PI of the CFC; Michelle Naughton, Co-PI of the CFC; Jacques Rossouw, Lead Project Officer; and Linda Pottern, Project Officer. Other routine participants on the PMC calls include Joanne Odenkirchen, Policy Analyst at NIH; Bernedine Lund, Technical Coordinator at the CCC; and Pam Nance, Project Manager at the CFC. The Committee held one to two conference calls per month from August 1995 through August 1996, with meetings on January 25 and May 1, 1996. Future scheduled contacts include six conference calls through the end of the 1996 and a meeting Nov. 4, 1996. The Nov. 4 meeting will focus on a review of the PMC goals and plans for the upcoming year, discussion on monitoring adherence and retention, and review of additional help that can be given to problem clinics.

Before each routine call, narrative summaries of performance for each clinic to be reviewed are circulated to all PMC members. The summaries include information from routine Level 1 monitoring activities by CCC lead staff liaisons as well as updated information about the functioning of the CC, and reports of current recruitment activities and adherence data. During the call, briefings on completed PMC visits and calls with clinics are given, materials received from CCs in response to specific PMC requests, action items from the previous call, and the clinic summaries are reviewed, and new action items are identified. After the call, a letter summarizing the PMC discussion is sent to the PI of the clinics reviewed on the call, pointing out areas of good performance and areas needing improvement.

The PMC reviewed all 40 clinics at least once by December 1995 and a second review of clinics will be completed by the end of 1996. Specific issues and clinics needing improvement are addressed more frequently.

During the six months from March 1 through August 31, 1996, the PMC conducted one Level 3 and eight Level 4 PMC visits to clinics. Four additional visits are scheduled through November, and a visit to two additional clinics is being scheduled for December-January. Three of the completed Level 4 visits were to clinics that had had a previous Level 3 visit. Subsequently, the PMC agreed that it would make at most one visit to each clinic for a particular problem area, and refer further issues to the Project Office. This separation of PMC and NIH site visits helps to clarify and maintain the CC enhancement function of the PMC visit and separate it from the contract issues addressed in NIH site visits. The PMC also agreed that after the PMC visits a clinic for a specific reason, for example, recruitment, it will not usually make a follow-up visit for the same issue. Rather, follow-up will be by phone, email, or mail, and any further visits to the clinic on that issue will be in the domain of the Project Office. In addition to PMC visits, the PMC has begun to hold conference calls with CCs where possible, rather than delaying a visit due to scheduling difficulties. This is especially effective when the CC has a specific issues that can be discussed on a call, for example, strategies for HRT-only recruitment. One PMC conference call was held with a CC in August and one call is scheduled in September.

After a PMC visit, the chair of the visit prepares a PMC Visit Report, describing the visit, the CC's strengths, issues review, and the PMC recommendations. A draft of the report is circulated to the PMC Visit members before being finalized and sent to the CC PI. Reports for all PMC visits through August have been completed and sent to the CCs.

During the face-to-face meeting on May 1, the committee reviewed the progress of the PMC to date and discussed how to monitor changes the CCs were asked to make following discussions on the PMC call and following a PMC visit. The following suggestions were made and implemented:

- To monitor the request and receipt of materials from the CCs, all requests are listed on a table showing date requested, date received, assigned PMC member, and date reviewed. This table is included and reviewed on each PMC call.

- To document the CC response to the PMC visit recommendations, a table listing the recommendations included in the PMC Visit report and the status of each of the recommendations is prepared. Beginning in July, these tables have been prepared and sent to the CCs, asking the CC to detail changes they have made.

- To solicit feedback on the PMC visit team's effectiveness, the PMC prepared a PMC Visit Survey, that will be sent to all CCs receiving a PMC visit after the final visit report has been sent. The survey asks for feedback on the content, format, and visitors of the visit, and asks for suggestions for changes.

It also came to the attention of the PMC that several CCs were scheduling screening visits for OS-only participants. To encourage the screening of CT women, the Project Office and CCC temporarily reduced the monthly OS enrollment goals by 35% to encourage CCs to focus on CT screening.

Two projects begun in the previous reporting period were finalized and sent out to the CCs.

- The Hot Tips booklet, containing generic problems and possible solutions, was finalized and distributed to the CCs in May.

- The Randomization Catch-up Plan spreadsheet that clinics can use as a template from which to monitor and project individual CC recruitment, screening, and follow-up activities was distributed to CC PIs and Clinic Managers in April. A second version of the Catch-up Plan spreadsheet, containing several updates to the participant follow-up schedule, CC-specific yields from screening visits, and a graph displaying the number of screening visits, CT and OS follow-up visits, is being prepared and will be distributed to the CCs in September. The Catch-up Plans have become a very useful tool for CCs to project the number of screening visits and mailings needed to reach their recruitment goals, and the Project Office plans to request that CCs include an updated Catch-up Plan with their quarterly reports to the Project Office.

Table 9.1
Clinical Center Performance Summary

CC Performance Summary
Data as of: 8/31/96

Summary - VCC

	Recruitment		HRT Follow-up		DM Follow-up		Retention		HRT Intervention		DM Intervention		CaD Intervention		Outcomes		Central Lab		Data		Overall	
	Jun.-Aug 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., Aug. 96	Rank
Atlanta	130	72	90	89	88	88	95	94	85	85	83	83		74		27	94	94	94	94	80	4
Birmingham	82	86	90	91	94	92	94	94	91	90	80	81		70		22	96	95	78	77	80	5
Bowman	126	64	73	76	80	78	95	94	85	85	81	80		69		6	95	96	92	91	74	16
Brigham	66	67	89	89	90	91	96	94	91	90	86	85		72		41	93	95	63	65	79	7
Buffalo	112	91	81	82	86	87	94	95	84	84	80	80		76		42	92	95	96	96	83	3
Chicago	88	74	72	75	71	73	97	96	88	89	88	85		61		25	97	97	84	81	76	12
Iowa	76	91	95	95	97	97	98	98	93	93	89	90		80		29	97	97	92	92	86	2
LaJolla	70	78	72	75	77	78	92	93	86	86	81	78		76		36	96	96	92	92	79	8
Memphis	72	90	82	83	82	83	95	95	90	89	86	85		71		23	92	92	64	64	77	11
Minneapolis	76	88	90	91	92	93	96	97	90	90	89	87		79		51	100	99	94	94	87	1
Newark	91	72	77	79	75	76	97	97	83	83	81	79		61		32	94	96	76	78	75	13
Pawtucket	79	60	76	78	72	74	94	94	88	88	90	86		71		22	97	97	80	80	75	14
Pittsburgh	86	74	71	70	74	71	97	98	93	93	88	89		74		23	96	96	88	87	77	10
Seattle	117	85	60	70	76	80	97	96	91	90	87	86		64		12	95	93	76	73	75	15
Tucson	163	94	75	69	80	73	94	93	85	84	81	79		67		38	93	91	91	90	78	9
UCDavis	123	87	80	83	84	86	96	96	89	89	81	81		73		29	98	96	75	75	80	6

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

Table 9.1 (continued)

CC Performance Summary
Data as of: 8/31/96

Summary - NCC

	Recruitment		HRT Followup		DM Followup		Retention		HRT Intervention		DM Intervention		CaD Intervention		Outcomes		Central Labs		Data		Overall	
	Jun.-Aug 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., May 96	cum., Aug 96	cum., Aug. 96	Rank
Chapel Hill	97	60	86	82	83	74		100		90	77	75					94	94	74	73	81	11
Chi-Rush	105	53	53	64	52	49		100		99	87	65					91	87	68	66	73	21
Cincinnati	52	53	90	88	83	90		99		98	86	80				47	83	89	85	80	80	12
Columbus	63	41	75	78	88	82		99		97	83	84				30	95	91	78	80	76	19
Detroit	32	29	65	47	96	52		98		33	69	70					88	94	80	80	63	24
Gainesville	85	88	86	91	86	90		98		97	93	90				60	88	97	96	96	90	2
GWU-DC	83	80	92	93	92	92		99		85	87	86				41	96	94	96	97	85	7
Honolulu	64	54	86	92	81	80		98		95	96	85				56	93	96	76	82	82	10
Houston	42	51	90	90	82	79		99		97	78	79				22	87	90	78	83	77	16
Irvine	82	49	73	50	63	65		99		80	70	77				27	96	97	66	61	67	23
LA	81	54	94	94	84	90		99		93	90	83				31	97	97	61	66	79	13
Madison	105	88	96	95	96	98		100		84	85	85				88	98	98	98	98	93	1
Mediantic	67	54	87	80	65	70		97		84	57	56				43	94	92	86	87	74	20
Miami	52	36	80	69	89	55		98		94	62	84				10	97	97	93	90	70	22
Milwaukee	79	78	97	93	98	95		100		98	90	88				55	96	96	96	95	89	5
Nevada	81	69	96	92	97	95		99		94	90	88				71	97	97	98	98	89	3
NY City	43	52	95	87	95	84		98		87	75	77				33	84	84	88	88	77	15
Oakland	88	68	90	85	84	78		99		92	73	79				77	95	93	77	79	83	8
Portland	58	56	83	83	95	79		99		90	93	88				47	95	94	52	53	76	17
San Antonio	79	61	84	80	71	74		98		93	78	78				13	88	92	94	94	76	18
Stanford	83	57	92	92	80	86		99		95	90	84					96	96	92	91	87	6
Stony Brook	74	48	99	98	99	92		99		95	67	80				94	95	96	98	98	89	4
Torrance	96	58	94	80	94	82		99		100	85	84				17	96	96	90	86	78	14
Worcester	61	56	90	88	83	81		98		95	90	85				59	90	90	92	88	82	9

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

Table 9.1 (continued)

Recruitment - VCC

	HRT[1] % goal			DM[1] % goal			Ca/D[2] % goal			OS[3] % goal			Age - HRT[4] % goal, 70 - 79			Age - DM[4] % goal, 70 - 79			Overall weighted average*			
	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Rank
Atlanta	62	114	65	146	233	99	69	74	79	83	50	99	23	84	29	105	156	46	85	130	72	13
Birmingham	64	69	88	90	122	97	92	33	108	97	151	129	37	64	43	39	106	40	72	82	86	7
Bowman	66	133	77	119	153	82	51	42	33	125	161	97	80	219	63	128	120	49	87	126	64	15
Brigham	46	56	59	106	103	99	96	75	66	71	81	77	7	28	36	13	25	49	65	66	67	14
Buffalo	93	109	79	104	103	97	120	62	96	185	166	187	40	166	73	25	157	59	93	112	91	3
Chicago	93	99	63	90	132	92	87	66	65	140	94	96	7	73	67	21	37	78	75	88	74	10
Iowa	85	77	109	71	80	81	127	67	103	101	163	109	131	69	86	70	50	48	96	76	91	2
LaJolla	70	58	76	131	90	85	94	64	74	159	186	118	49	21	67	67	59	68	92	70	78	9
Memphis	99	71	93	129	71	94	118	72	113	93	137	99	83	46	62	89	67	50	107	72	90	4
Minneapolis	108	89	79	90	56	104	104	104	106	136	147	133	119	37	52	94	33	48	104	76	88	5
Newark	46	74	59	159	132	101	79	97	67	180	166	176	41	29	30	87	55	42	92	91	72	12
Pawtucket	61	78	60	81	123	73	59	45	58	243	180	126	45	23	34	40	64	33	72	79	60	16
Pittsburgh	63	76	63	143	154	96	75	59	60	40	59	190	60	46	42	83	74	51	85	86	74	11
Seattle	181	149	94	63	102	85	105	68	68	136	149	115	159	172	96	83	107	72	118	117	85	8
Tucson	88	117	67	145	183	107	113	60	90	138	142	173	166	218	83	187	379	101	131	163	94	1
UCDavis	71	118	76	99	119	104	102	113	82	179	139	151	53	139	62	87	136	82	91	123	87	6
*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 9.1 (continued)

Recruitment - NCC

	HRT[1] % goal			DM[1] % goal			Ca/D[2] % goal			OS[3] % goal			Age - HRT[4] % goal, 70 - 79			Age - DM[4] % goal, 70 - 79			Overall weighted average*			
	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Mar. - May	Jun. - Aug.	cum., Aug. 96	Rank
Chapel Hill	54	117	53	126	137	95	23	46	40	61	140	110	22	86	34	66	66	42	62	97	60	8
Chi-Rush	90	169	78	85	142	70	0	13	9	225	85	123	29	86	35	25	116	39	61	105	53	17
Cincinnati	49	53	46	80	64	66	79	41	51	92	103	108	70	41	38	62	36	32	70	52	53	16
Columbus	43	54	34	99	118	74	0	29	21	97	158	105	29	22	15	50	33	24	48	63	41	22
Detroit	29	43	50	23	50	36	0	10	7	103	18	70	7	29	19	4	25	8	19	32	29	24
Gainesville	115	112	113	59	81	76	121	77	88	159	162	191	95	57	66	22	47	36	93	85	88	1
GWU-DC	85	77	73	71	74	89	122	67	81	160	239	211	58	94	59	33	58	32	85	83	80	3
Honolulu	77	36	49	123	156	82	53	17	26	189	135	141	65	7	41	37	54	38	83	64	54	13
Houston	27	25	50	36	55	57	70	45	51	80	97	118	57	20	23	69	37	36	51	42	51	19
Irvine	90	97	54	120	127	73	0	0	0	158	279	168	65	79	46	50	33	29	72	82	49	20
LA	76	85	60	66	124	71	17	43	36	141	92	115	36	79	46	17	58	25	52	81	54	14
Madison	146	151	108	99	97	98	30	69	59	198	220	186	86	94	74	54	54	54	93	105	88	2
Medlantic	50	74	58	70	80	71	23	42	37	95	139	98	43	72	43	50	33	32	50	67	54	15
Miami	79	101	59	67	86	51	0	8	6	56	28	60	50	7	20	45	33	22	49	52	36	23
Milwaukee	126	108	97	104	99	98	17	76	61	187	88	118	86	43	58	33	21	38	83	79	78	4
Nevada	104	122	82	74	81	76	36	61	54	206	142	165	72	58	50	29	33	29	75	81	69	5
NY City	64	40	58	36	50	63	26	28	28	152	176	175	19	26	31	18	18	27	43	43	52	18
Oakland	85	106	71	124	128	92	43	43	43	163	155	183	29	72	45	37	45	33	76	88	68	6
Portland	58	54	55	105	102	95	23	43	38	142	110	75	29	14	28	33	25	36	59	58	56	11
San Antonio	104	144	86	81	86	67	83	56	63	73	70	75	58	43	30	33	25	23	78	79	61	7
Stanford	95	97	71	95	89	74	0	19	15	166	142	147	64	129	52	44	98	42	67	83	57	10
Stony Brook	65	85	53	42	104	60	23	35	32	110	117	123	14	72	28	12	54	27	40	74	48	21
Torrance	53	89	54	69	147	75	35	48	45	164	131	144	19	58	27	28	127	46	52	96	58	9
Worcester	63	36	46	111	106	85	33	30	31	159	206	167	36	22	32	37	54	36	67	61	56	12
*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 9.1 (continued)

Minority Randomization/Enrollment at Pool 1 Clinics

	% Non-white HRT/DM/OS[1]		
VCCs	cum. May 96	cum. Aug. 96	Rank
Atlanta	28	28	8
Birmingham	41	44	4
LaJolla	29	28	8
Tucson	20	20	10
NCCs			
Chi-Rush	68	71	1
Detroit	38	37	5
Honolulu	72	70	2
Medlantic	64	65	3
Miami	28	34	6
San Antonio	30	32	7

[1] Derived from WHIP0960. Distributed in Monthly Activity Reports. Can be run at CC as WHIP777.

Table 9.1 (continued)

HRT Follow-up - VCC

	6 Week[1]		Semi-Annual 1[2]						Annual Visit 1[2]						Semi-Annual 2[2]						Annual Visit 2[2]						Overall		
	Conducted		Conducted		+/- 2 wks		Complete		Conducted		+/- 2 wks		Complete		Conducted		+/- 2 wks		Complete		Conducted		+/- 2 wks		Complete				
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Atlanta	94	94	99	99	92	93	84	85	99	99	96	96	75	74	92	94	86	87	83	84		91		89		68	90	89	5
Birmingham	90	92	98	98	87	87	92	92	98	99	85	85	84	84	97	98	91	89	84	84	100	100	83	90	83	83	90	91	3
Bowman	93	93	94	94	77	80	80	83	92	92	57	62	68	66	77	82	42	48	70	76	81	85	53	63	59	59	73	76	11
Brigham	95	94	100	99	92	92	86	88	99	99	93	93	82	79	95	97	87	91	80	79	92	88	92	86	69	70	89	89	4
Buffalo	97	96	95	96	84	85	83	83	95	96	83	83	72	74	82	90	66	71	74	75	87	90	67	68	62	60	81	82	8
Chicago	90	90	95	96	63	64	83	82	97	96	59	58	65	67	89	87	55	53	73	77	70	79	30	37	71	87	72	75	13
Iowa	100	100	100	99	95	95	95	96	99	100	93	93	91	91	99	99	93	94	89	90	100	98	98	95	83	87	95	95	1
LaJolla	85	87	89	91	72	74	75	76	87	88	66	68	69	69	81	81	56	62	78	78	72	80	53	60	58	60	72	75	12
Memphis	87	88	97	98	85	85	79	79	97	97	91	89	58	56	94	92	80	76	75	75	92	95	84	81	46	65	82	83	7
Minneapolis	100	100	100	100	88	89	90	90	99	100	90	92	82	83	98	100	85	87	78	76	100	98	82	84	84	81	90	91	2
Newark	92	90	94	94	65	64	80	81	96	96	77	75	63	67	83	87	42	47	68	72	96	96	78	77	65	76	77	79	9
Pawtucket	94	95	93	93	77	78	86	86	93	95	39	45	72	71	88	90	54	56	73	71	91	91	65	73	63	71	76	78	10
Pittsburgh	90	90	98	98	82	81	92	91	95	90	52	47	61	60	91	91	64	52	79	80	73	85	16	10	35	32	71	70	15
Seattle	90	94	90	95	56	52	84	90	88	92	53	53	65	74	85	86	23	23	61	74	54	79	6	27	22	72	60	70	14
Tucson	68	77	91	91	65	63	79	78	95	93	69	68	57	54	84	83	70	59	70	70	94	76	81	43	53	47	75	69	16
UCDavis	98	99	97	97	85	85	72	83	95	95	68	67	74	75	88	89	80	81	68	77	89	86	54	66	68	78	80	83	6

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.
Complete = % of visits conducted for which all expected tasks have been key-entered. Specifically,
Semi-Annual Contact 1: tasks 10, 33, 950, 951
Annual Visit 1: tasks 10, 33, 38, 44, 45, 80, 81, 84, 100, 950, 951
Semi-Annual Contact 2: tasks 10, 33, 950, 951
Annual Visit 2: tasks 10, 33, 80, 81, 84, 950, 951

[1] From WHIP1131. Can be run at CC as WHIP0781 or WHIP0786.
[2] From WHIP1141, distributed in Monthly Activity Reports.

Table 9.1 (continued)

HRT Follow-up - NCC

	6 Week[1]		Semi-Annual 1[2]						Annual Visit 1[2]						Semi-Annual 2[2]						Annual Visit 2[2]						Overall		
	Conducted		Conducted		+/- 2 wks		Complete		Conducted		+/- 2 wks		Complete		Conducted		+/- 2 wks		Complete		Conducted		+/- 2 wks		Complete				
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Chapel Hill	97	92	100	100	79	74	67	76		93		71		69													86	82	16
Chi-Rush	87	80	53	89	21	19	50	67																			53	64	22
Cincinnati	94	95	96	97	89	89	81	85		96		88		70													90	88	11
Columbus	93	96	90	98	55	74	61	42																			75	78	20
Detroit	69	64	96	96	9	74	86	79		17		0		0													65	47	24
Gainesville	96	97	98	99	92	93	91	94	83	93	61	74	84	83													86	91	9
GWU-DC	99	100	99	99	81	89	87	91		98		91		80													92	93	5
Honolulu	93	94	97	99	100	97	53	71		93		93		100													86	92	8
Houston	99	99	94	96	84	84	96	94	100	95	100	89	54	72													90	90	10
Irvine	71	46	73	83	63	45	86	77		70		30		0													73	50	23
LA	99	99	95	99	100	88	80	84		93		93		100													94	94	3
Madison	98	98	99	100	96	97	92	94		100		88		85													96	95	2
Medlantic	98	98	90	97	76	62	83	84		89		64		69													87	80	17
Miami	95	85	84	81	60	54	81	86		81		63		31													80	69	21
Milwaukee	99	98	99	99	96	91	93	94		100		79		93													97	93	4
Nevada	96	94	100	98	93	93	95	94		93		90		85													96	92	7
NY City	97	96	99	97	87	91	96	94		83		75		70													95	87	13
Oakland	98	98	96	98	75	82	92	91		100		71		53													90	85	14
Portland	92	96	98	99	53	82	90	90		95		79		39													83	83	15
San Antonio	66	68	91	90	94	76	86	86		94		74		70													84	80	19
Stanford	98	95	92	100	100	86	79	88																			92	92	6
Stony Brook	100	100	100	99	100	99	95	97		100		100		94													99	98	1
Torrance	96	89	98	93	90	86	90	87		75		70		60													94	80	18
Worcester	84	88	95	96	100	82	79	88																			90	88	12

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.
Complete = % of visits conducted for which all expected tasks have been key-entered. Specifically,
Semi-Annual Contact 1: tasks 10, 33, 950, 951
Annual Visit 1: tasks 10, 33, 38, 44, 45, 80, 81, 84, 100, 950, 951
Semi-Annual Contact 2: tasks 10, 33, 950, 951
Annual Visit 2: tasks 10, 33, 80, 81, 84, 950, 951

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

Table 9.1 (continued)

Retention - VCC

	HRT[1]				DM[2]				CaD[3]				OS				
	% Continuing Intervention		% Continuing Followup		% Continuing Intervention		% Continuing Followup		% Continuing Intervention		% Continuing Followup		% Continuing Followup		Overall		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Atlanta	83	82	99	98	99	99	99	99		86		100			95	94	13
Birmingham	83	80	99	99	97	97	99	99		89		100			94	94	12
Bowman	87	86	97	97	99	97	98	97		90		99			95	94	11
Brigham	87	86	99	98	99	98	99	99		85		100			96	94	10
Buffalo	83	83	99	99	97	97	99	99		90		100			94	95	9
Chicago	90	91	99	99	98	98	99	98		93		96			97	96	7
Iowa	93	93	99	100	99	99	99	100		95		100			98	98	1
LaJolla	85	82	95	95	91	94	96	96		92		99			92	93	16
Memphis	91	90	99	99	92	92	98	98		91		100			95	95	8
Minneapolis	90	90	100	100	96	97	99	100		93		100			96	97	3
Newark	91	91	99	99	100	100	99	100		90		100			97	97	4
Pawtucket	83	83	98	98	96	96	99	99		87		99			94	94	14
Pittsburgh	89	89	99	99	100	100	99	100		98		100			97	98	2
Seattle	91	89	99	98	98	98	99	99		94		100			97	96	5
Tucson	84	84	98	98	94	94	99	99		86		99			94	93	15
UCDavis	90	90	98	98	97	97	98	98		94		100			96	96	6

Notes: Continuing Intervention = % of randomized participants (intervention participants for DM) with follow-up status 1 - 4 on Form 7.
Continuing Follow-up = % of randomized participants with "active intervention" status.

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

Table 9.1 (continued)

Retention - NCC

	HRT[1]				DM[2]				CaD[3]				OS			
	% Continuing Intervention		% Continuing Followup		% Continuing Intervention		% Continuing Followup		% Continuing Intervention		% Continuing Followup		% Continuing Followup		Overall	
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96
Chapel Hill		99		100		100		100		100		100				100
Chi-Rush		100		100		100		100								100
Cincinnati		95		100		100		100		99		100				99
Columbus		96		100		100		100		100		100				99
Detroit		95		99		96		100								98
Gainesville		95		99		99		100		97		99				98
GWU-DC		94		100		100		99		100		100				99
Honolulu		97		99		96		100		97		100				98
Houston		94		100		100		100		100		100				99
Irvine		96		100		100		100								99
LA		94		99		100		100		98		100				99
Madison		97		100		100		100		100		100				100
Medlantic		91		99		93		100		100		100				97
Miami		97		99		96		100								98
Milwaukee		99		100		100		100		100		100				100
Nevada		96		100		98		99		100		100				99
NY City		93		98		98		99		98		100				98
Oakland		98		100		100		100		98		100				99
Portland		96		99		100		100		98		100				99
San Antonio		95		99		100		100		96		99				98
Stanford		97		100		100		100		96		100				99
Stony Brook		97		100		99		100		100		100				99
Torrance		99		99		100		99		95		100				99
Worcester		92		100		100		100		93		100				98

Notes: Continuing Intervention = % of randomized participants (intervention participants for DM) with follow-up status 1 - 4 on Form 7.
Continuing Follow-up = % of randomized participants with "active intervention" status.

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

Table 9.1 (continued)

HRT Intervention - VCC

	% Women ≥ 80% Adherent[1] at Annual Visit		% Women with Pill Count at Annual Visit[2]		% Blinding[3]		Overall weighted ave*		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Atlanta	77	77	89	88	93	93	85	85	13
Birmingham	88	87	92	91	95	94	91	90	4
Bowman	82	82	83	83	97	97	85	85	12
Brigham	89	90	90	88	96	95	91	90	3
Buffalo	79	80	84	85	92	91	84	84	14
Chicago	85	84	88	90	97	96	88	89	9
Iowa	92	92	95	95	92	91	93	93	1
LaJolla	80	80	87	88	95	94	86	86	11
Memphis	87	85	91	90	96	95	90	89	7
Minneapolis	85	85	92	92	95	94	90	90	6
Newark	75	75	88	88	91	90	83	83	16
Pawtucket	85	84	89	89	93	93	88	88	10
Pittsburgh	91	90	92	92	99	99	93	93	2
Seattle	88	86	90	90	98	98	91	90	4
Tucson	81	81	81	80	99	96	85	84	15
UCDavis	85	86	90	90	94	93	89	89	7
*Weights	1		1		0.5				

[1] Adherent as measured by pill count or estimate at annual visit 1, excluding ERT→PERT participants. From data analysis, not yet routinely distributed to CCs.

[2] % of Annual Visit 1s conducted that include study pill collections. From WHIP1141, distributed in Monthly Activity Reports.

[3] % Blinding = % of ppts for whom no unblinding occured. From DSMB report not distributed to CCs.

Table 9.1 (continued)

HRT Intervention - NCC

	% Women ≥ 80% Adherent[1] at Annual Visit		% Women with Pill Count at Annual Visit[2]		% Blinding[3]		Overall weighted ave*		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Chapel Hill		77		100		98		90	17
Chi-Rush						99		99	2
Cincinnati		100		96		96		98	4
Columbus						97		97	6
Detroit				0		98		33	24
Gainesville		96		98		98		97	5
GWU-DC		84		80		95		85	20
Honolulu		92		100		92		95	8
Houston		97		95		99		97	7
Irvine				71		98		80	23
LA		92		93		95		93	14
Madison		74		88		95		84	22
Medlantic		75		86		98		84	21
Miami		100		85		99		94	12
Milwaukee		100		96		97		98	3
Nevada		96		89		98		94	13
NY City		78		90		97		87	19
Oakland		82		100		95		92	16
Portland		82		94		96		90	18
San Antonio		91		91		100		93	15
Stanford						95		95	9
Stony Brook		94		94		97		95	11
Torrance		100		100		98		100	1
Worcester						95		95	9
*Weights		1		1		0.5			

[1] Adherent as measured by pill count or estimate at annual visit 1, excluding ERT→PERT participants. From data analysis, not yet routinely distributed to CCs.

[2] % of Annual Visit 1s conducted that include study pill collections. From WHIP1141, distributed in Monthly Activity Reports.

[3] % Blinding = % of ppts for whom no unblinding occured. From DSMB report not distributed to CCs.

Table 9.1 (continued)

DM Intervention - VCC

	Adherence (Session 12)																		
	Timeliness of group formation[1]		Performance				Fat Gram						Fruit/Veg		Grain		Summary		
			% Attendance[2]		% Complete[3]		% Collected[4]		% < goal[5]		% < goal +5 g[6]		% Collected[4]		% Collected[4]		weighted ave*		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Atlanta	93	93	69	68	90	90	83	83	77	76	88	87	83	83	83	83	83	83	9
Birmingham	83	81	64	64	88	90	82	84	74	74	89	89	81	83	81	83	80	81	11
Bowman	91	89	72	69	88	87	74	73	73	74	89	89	74	73	74	73	81	80	13
Brigham	90	88	74	73	94	93	91	89	76	76	90	91	91	89	91	89	86	85	6
Buffalo	87	86	77	77	95	94	79	80	62	62	81	82	79	80	79	80	80	80	12
Chicago	90	89	87	78	90	90	95	91	73	72	89	89	92	91	92	91	88	85	6
Iowa	82	81	74	74	99	100	95	97	86	86	96	96	97	97	97	97	89	90	1
LaJolla	81	74	72	69	90	88	77	76	78	75	91	89	77	76	77	76	81	78	16
Memphis	95	93	79	69	90	91	87	87	78	78	89	89	87	87	87	87	86	85	8
Minneapolis	96	96	80	78	95	92	93	89	76	75	93	92	93	89	93	89	89	87	3
Newark	94	93	62	58	89	87	79	75	75	72	90	89	79	74	79	74	81	79	15
Pawtucket	92	91	86	71	96	91	95	89	78	77	94	93	90	89	90	89	90	86	5
Pittsburgh	93	95	74	75	97	97	87	88	85	84	94	93	88	89	87	88	88	89	2
Seattle	93	92	77	76	93	93	82	82	84	84	94	93	81	80	81	80	87	86	4
Tucson	82	77	68	63	95	91	84	82	70	70	87	88	79	82	79	82	81	79	14
UCDavis	88	87	66	66	92	91	80	80	75	74	88	88	80	80	80	80	81	81	10
*weights:	1		1		1		1		1		1		0.25		0.25				

[1] Timeliness of group formation = % women randomized to DM intervention who started intervention within 20 weeks of randomization or have been waiting less than 20 weeks but have not yet started intervention. Derived from WHIP1110 and WHIP1118, which are distributed with CC Monthly Activity Reports.

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

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

[4] % collected = 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.

[5] % of women with fat scores equal to or less than their fat gram goals. From data analysis not yet routinely distributed to CCs.

[6] % of women with fat scores equal to or less than their fat gram goals + five grams. From data analysis not yet routinely distributed to CCs.

Table 9.1 (continued)

DM Intervention - NCC

	Timeliness of group formation[1]		Adherence (Session 12) Performance % Attendance[2]		Performance % Complete[3]		Fat Gram % Collected[4]		Fat Gram % < goal[5]		Fat Gram % < goal +5 g[6]		Fruit/Veg % Collected[4]		Grain % Collected[4]		Summary weighted ave*		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Chapel Hill	93	86	58	48	84	87	74	78	64	61	93	89	74	78	74	78	77	75	21
Chi-Rush	87	82		71		71		47		50		75		47		47	87	65	23
Cincinnati	87	85	76	66	98	95	93	80	67	63	90	88	93	80	93	80	86	80	15
Columbus	97	92	62	68	100	88	85	88	64	73	91	91		88		88	83	84	11
Detroit	89	87	52	54	63	68	63	68	65	63	82	79		68		68	69	70	22
Gainesville	86	78	86	82	96	95	93	93	95	92	100	97	95	93	95	93	93	90	1
GWU-DC	91	87	80	76	89	91	82	86	85	80	98	98	82	86	82	86	87	86	5
Honolulu	98	90	100	80	100	86	92	83	91	76	100	93	92	83	92	83	96	85	8
Houston	88	91	61	65	84	86	82	82	64	63	86	83	82	82	82	82	78	79	17
Irvine	95	95	64	64	64	79	64	79	56	64	78	82		79		79	70	77	19
LA	97	92	77	70	100	93	95	86	71	66	100	92		86		86	90	83	13
Madison	93	92	68	74	98	99	95	97	66	66	84	79	95	97	95	97	85	85	6
Mediantic	81	71	37	35	54	61	34	45	71	59	79	73	34	45	34	45	57	56	24
Miami	85	73		67		94		89	0	82	100	94		89		89	62	84	12
Milwaukee	96	92	78	81	100	95	100	92	74	74	94	91		92		92	90	88	4
Nevada	96	94	74	71	93	93	86	86	92	90	97	96		86		86	90	88	3
NY City	100	95	65	56	79	84	72	85	56	60	78	79	72	85	72	85	75	77	20
Oakland	94	83	76	75	76	90	64	72	56	70	69	86		72		72	73	79	16
Portland	97	95	86	79	100	100	94	96	85	69	97	87	94	96	94	96	93	88	2
San Antonio	91	88	55	55	79	83	74	74	77	77	94	94	74	74	74	74	78	78	18
Stanford	96	93	87	72	93	91	73	79	91	82	100	91		79		79	90	84	9
Stony Brook	79	79	50	62	80	92	50	86	60	74	80	86		86		86	67	80	14
Torrance	93	90	71	71	92	93	92	87	65	69	96	92		87		87	85	84	10
Worcester	93	91	79	76	95	89	95	84	83	79	94	90	95	84	95	84	90	85	7
*weights:			1		1		1		1		1		0.25		0.25				

[1] Timeliness of group formation = % women randomized to DM intervention who started intervention within 20 weeks of randomization or have been waiting less than 20 weeks but have not yet started intervention. Derived from WHIP1110 and WHIP1118, which are distributed with CC Monthly Activity Reports.

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

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

[4] % collected = 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.

[5] % of women with fat scores equal to or less than their fat gram goals. From data analysis not yet routinely distributed to CCs.

[6] % of women with fat scores equal to or less than their fat gram goals + five grams. From data analysis not yet routinely distributed to CCs.

Table 9.1 (continued)

CaD Intervention - VCC

	% Women ≥ 80% Adherent[1] at SAV- 2		% Women with Pill Count at SAV-2[2]		Overall Average		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Atlanta		55		92		74	6
Birmingham		43		97		70	11
Bowman		49		89		69	12
Brigham		67		76		72	8
Buffalo		61		90		76	4
Chicago		65		57		61	15
Iowa		62		98		80	1
LaJolla		67		85		76	3
Memphis		49		92		71	10
Minneapolis		82		75		79	2
Newark		51		70		61	16
Pawtucket		53		89		71	9
Pittsburgh		62		86		74	5
Seattle		61		66		64	14
Tucson		58		76		67	13
UCDavis		59		87		73	7

[1] Adherent as measured by pill count or estimate at Semi-Annual Visit 2. From data analysis, not yet routinely distributed to CCs.

[2] % of Semi-Annual Visit 2s conducted that include study pill collections. From WHIP1143, distributed in Monthly Activity Reports.

Table 9.1 (continued)

Central Laboratory - VCC

	ECGs		Blood		4DFRs				
	Grade % grades 1 - 3[1]		% Complete[2]		% < 4 Errors[3]		Summary average		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Atlanta	91	91	93	93	99	98	94	94	13
Birmingham	92	93	95	95	98	98	96	95	10
Bowman	90	91	95	96	100	100	95	96	8
Brigham	95	95	94	94	98	97	93	95	10
Buffalo	95	95	97	96	96	95	92	95	10
Chicago	93	93	98	98	100	100	97	97	2
Iowa	92	93	98	98	100	100	97	97	2
LaJolla	90	91	97	97	100	99	96	96	8
Memphis	89	89	87	86	95	100	92	92	15
Minneapolis	99	99	100	100	100	98	100	99	1
Newark	94	94	97	97	97	98	94	96	5
Pawtucket	91	91	99	99	100	100	97	97	4
Pittsburgh	90	90	98	98	100	100	96	96	6
Seattle	90	90	95	95	96	95	95	93	14
Tucson	86	86	92	93	93	93	93	91	16
UCDavis	95	95	99	99	93	94	98	96	6

[1] % ECGs of acceptable quality (grades 1 - 3). Derived from WHIP1023. Distributed in CC Monthly QA Reports.

[2] % Complete blood aliquots, based on aliquots required for visit type. From WHIP1044. Distributed in CC Monthly QA Reports.

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

Table 9.1 (continued)

Central Laboratory - NCC

	ECGs		Blood		4DFRs		Summary		
	Grade % grades 1 - 3[1]		% Complete[2]		% < 4 Errors[3]		average		
	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	cum., May 96	cum., Aug. 96	Rank
Chapel Hill	90	91	91	91	100	100	94	94	13
Chi-Rush	97	98	76	80	100	83	91	87	23
Cincinnati	94	95	89	88	75	85	83	89	22
Columbus	96	95	90	91	75	88	95	91	19
Detroit	94	94	86	87	100	100	88	94	15
Gainesville	94	94	97	97	100	100	88	97	3
GWU-DC	88	89	99	99	100	95	96	94	12
Honolulu	95	95	98	98	90	95	93	96	8
Houston	96	97	68	73	100	100	87	90	20
Irvine	98	98	93	94	100	100	96	97	2
LA	96	96	95	95	100	100	97	97	3
Madison	96	96	98	98	100	100	98	98	1
Medlantic	85	86	96	96	100	93	94	92	18
Miami	93	93	98	98	100	100	97	97	3
Milwaukee	93	93	96	96	100	100	96	96	7
Nevada	91	91	99	99	100	100	97	97	6
NY City	81	82	97	97	69	74	84	84	24
Oakland	91	91	94	93	100	95	95	93	16
Portland	95	95	89	87	100	100	95	94	13
San Antonio	94	93	91	91	89	93	88	92	17
Stanford	91	91	96	96	100	100	96	96	11
Stony Brook	92	94	94	94	100	100	95	96	8
Torrance	93	93	96	95	100	100	96	96	8
Worcester	93	94	97	98	83	78	90	90	20

[1] % ECGs of acceptable quality (grades 1 - 3). Derived from WHIP1023. Distributed in CC Monthly QA Reports.
[2] % Complete blood aliquots, based on aliquots required for visit type. From WHIP1044. Distributed in CC Monthly QA Reports.
[3] % archived 4DFRs with < 4 errors, cum. from Jan. 1, 1995. Derived from WHIP0935. Distributed to CCs quarterly.

Table 9.1 (continued)

Data Management - VCC

	Timeliness of key-entry[1]		
	cum., May 96	cum., Aug. 96	Rank
Atlanta	94	94	2
Birmingham	78	77	12
Bowman	92	91	6
Brigham	63	65	15
Buffalo	96	96	1
Chicago	84	81	9
Iowa	92	92	5
LaJolla	92	92	4
Memphis	64	64	16
Minneapolis	94	94	3
Newark	76	78	11
Pawtucket	80	80	10
Pittsburgh	88	87	8
Seattle	76	73	14
Tucson	91	90	7
UCDavis	75	75	13

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

Table 9.1 (continued)

Data Management - NCC

	Timeliness of key-entry[1]		
	cum., May 96	cum., Aug. 96	Rank
Chapel Hill	74	73	20
Chi-Rush	68	66	21
Cincinnati	85	80	17
Columbus	78	80	17
Detroit	80	80	16
Gainesville	96	96	5
GWU-DC	96	97	4
Honolulu	76	82	15
Houston	78	83	14
Irvine	66	61	23
LA	61	66	22
Madison	98	98	1
Medlantic	86	87	12
Miami	93	90	9
Milwaukee	96	95	6
Nevada	98	98	3
NY City	88	88	11
Oakland	77	79	19
Portland	52	53	24
San Antonio	94	94	7
Stanford	92	91	8
Stony Brook	98	98	1
Torrance	90	86	13
Worcester	92	88	10

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

Table 9.1 (continued)

CC Performance Summary
Data as of: 8/31/96

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 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Rank[8]
Atlanta		95		82		74		84		71		77		76		82				27	9
Birmingham		97		75		100		100		35		54		67		58				22	14
Bowman		83		90		15		71		82		84		84		84				6	16
Brigham		97		93		94		68		63		83		96		57				41	3
Buffalo		94		93		92		96		84		87		90		78				42	2
Chicago		89		79		92		93		74		85		98		91				25	10
Iowa		99		89		62		80		79		96		77		50				29	8
LaJolla		84		85		60		97		76		94		26		13				36	5
Memphis		89		80		65		95		93		98		91		73				23	12
Minneapolis		98		93		90		92		87		94		87		62				51	1
Newark		85		81		52		84		76		96		95		85				32	6
Pawtucket		86		30		24		83		87		99		98		88				22	13
Pittsburgh		88		39		63		98		89		91		96		74				23	11
Seattle		91		93		0		100		100		100		73		69				12	15
Tucson		88		86		77		91		69		85		82		63				38	4
UCDavis		90		91		45		80		80		100		90		82				29	7

[1] Initial Form 33 mailings from CCC to OS participants was delayed approximately 6 months.
[2] Only Form 33, ver. 3 starting March 1996 require Form 33D.
[3] Excludes closed cases for which no documents were requested.
[4] % cases assigned of those for which documents were requested.
[5] % cases adjudication within 12 weeks or have been waiting less than 12 weeks but not yet sent to local adjudication.
[6] % adjudicated within 14 days or have been waiting less than 14 days but have not yet been adjudicated.
[7] % closed within 14 weeks of Form 33 or have been waiting less than 14 weeks from Form 33 .
[8] Rank based on overall timeliness.

Table 9.1 (continued)

CC Performance Summary
Data as of: 8/31/96

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 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Cum. May 96	Cum. Aug 96	Rank[8]
Chapel Hill		89		74		20		79													
Chi-Rush		75		24																47	9
Cincinnati		97		82		59		89												30	15
Columbus		93		87		25															
Detroit		80		0																60	5
Gainesville		97		84		20		83		50		75		79		64				41	12
GWU-DC		98		81		4		86		100		100		85		85				56	7
Honolulu		95		77		48		82		0		67								22	17
Houston		91		74		19		0		70		80								27	16
Irvine		75		52		0														31	14
LA		94		86		13														88	2
Madison		100		87		91		79		53		91		94		81				43	11
Mediantic		91		75		21		100		100		100		100		100				10	20
Miami		67		16																55	8
Milwaukee		98		88		100		21		11		71								71	4
Nevada		97		85		55		98		14		90								33	13
NY City		92		71		42		100		60		50		50		50				77	3
Oakland		85		87		74		40		0		94								47	10
Portland		95		93		46		78												13	19
San Antonio		85		77		100		64		23		73									
Stanford		97		27		50		36		17		92								94	1
Stony Brook		99		84		82		90		34		93		100		100				17	18
Torrance		89		85		5														59	6
Worcester		93		90		52		9		6		50									

[1] Initial Form 33 mailings from CCC to OS participants was delayed approximately 6 months.
[2] Only Form 33, ver. 3 starting March 1996 require Form 33D.
[3] Excludes closed cases for which no documents were requested.
[4] % cases assigned of those for which documents were requested.
[5] % cases adjudication within 12 weeks or have been waiting less than 12 weeks but not yet sent to local adjudication.
[6] % adjudicated within 14 days or have been waiting less than 14 days but have not yet been adjudicated.
[7] % closed within 14 weeks of Form 33 or have been waiting less than 14 weeks from Form 33 .
[8] Rank based on overall timeliness.

10. Timeline

WHI Manuals, *Vol. 1 - Study Protocol and Polices, Protocol Section 11 - Timetable* defines the study timeline, reflecting the progress and expectations as of August, 1994. The official startup of all activities has be implemented on schedule with the exception of OS and CaD recruitment. The delay in OS for Office of Management and Budget approval created problems for VCCs in managing CT ineligible women and in planning VCC operations to achieve full OS recruitment within the recruitment timeline. To address this issue, in August 1994, the NIH Project Office agreed to extend VCC recruitment period for OS for one year.

The delay in CaD start-up was a result of difficulties in obtaining the supplements from the manufacturer. This results in a small loss in the expected person-years of observation as about 2,800 women were randomized in the CT (HRT/DM) more than 1 year before CaD was officially open and thus they missed the scheduled randomization at the first year follow-up visit. Since these women were offered CaD participation at the second annual visit, the total loss in person years associated with this delay is small.

The startup of the NCCs has been similar to the VCC experience. Though the NCCs appeared to get off the mark more quickly than VCCs their recruitment curve is now quite similar to the VCC's. NCCs are being strongly encouraged to be as aggressive as possible in meeting their goals and in making up existing deficits. In particular, NCCs are being strongly encouraged to stress CT recruitment over OS.

To meet the shortfall in recruitment created by the funding of 40 CCs rather than 45, 15 CCs have been funded for increased recruitment (see *Section 2.2*). This additional recruitment will extend these VCCs' recruitment efforts through the NCC recruitment period (1998), and accounts for the equivalent of 4.25 additional CCs recruiting for DM, 5.25 recruiting for HRT and 4.75 recruiting for OS. (See *Figure 2.1 - Enhanced Recruitment Sites.*)

With the original end of VCC recruitment scheduled for August 31, 1996 (still applicable for those not pursuing enhanced recruitment), we projected some modest shortfalls in VCC recruitment into HRT and DM. The majority of VCCs without enhanced recruitment appear to have an adequate population base to achieve their goals so the Steering Committee elected to modify the definition of the end of recruitment (i.e., women in the pipeline by the end of the recruitment period may complete screening and be randomized) and to extend HRT recruitment for six months. In addition, all clinics with the ability to recruit above existing goals within age cells with anticipated shortfalls studywide were given additional encouragement to do so. Thus all VCCs are expected to continue active recruitment efforts during the next six months. This additional flexibility is needed to handle the tremendous workload of the clinics who are trying to finish recruitment while conducting follow-up, intervention, and outcome activities for a large number of women.

During the next six months, NCCs and VCCs with enhanced recruitment will continue their emphasis on recruitment even while they take on an increasing load of follow-up activities, interventions and outcomes processing. These combined requirements place a very heavy burden on

clinic operations and staff. To provide some assistance another streamlining effort is planned to help improve efficiency.

The CCC will be working with CCs on predicting and improving adherence and retention, further development of DM maintenance activities, and refining the procedures for outcomes documentation and adjudication.

The CCC will also be continuing the centralized follow-up of OS women begun in April 1996 and beginning the analysis of stored blood specimens. Additional efforts on quality assurance, substudy procedures and analyses, trial monitoring and reporting, and manuscript publications are also underway.

11. Design and Power

Clinical Trial power calculations were based on assumptions involving the accrual rates, baseline characteristics, adherence to intervention (drop-outs) and control (drop-ins or drift), loss to follow-up, and incidence rates in the control groups, as well as the hypothesized intervention effects. See *Appendix 2-A3* of the WHI protocol (WHI Manuals, *Vol. 1 - Study Protocol and Policies, Section 1-A3 - Statistical Power for WHI Clinical Trial and Observational Trial*) for more details.

Table 11.1 - Design Assumptions and Current Estimates summarizes the design parameters under the current protocol and the related observable quantities. As noted in earlier sections, the data are not adequate yet to provide useful estimates of some parameters related to follow-up.

The lag in accrual and the under-recruitment of women aged 70-79 has been presented and discussed among WHI Investigators. Defining the end of recruitment to allow women in the pipeline by the end of recruitment to complete screening and extending HRT recruitment by 6 months should allow VCCs without enhanced recruitment to meet their overall goals if they can meet their current monthly goals. Vanguard Clinical Centers with enhanced recruitment and NCCs have 17 months to the end of recruitment as defined above. This timeline is achievable if the recent surge can be maintained. If recruitment proceeds at the pace of meeting monthly goals we would expect to meet DM goals in May 1998 and HRT goals in July 1998.

Table 11.2 - Sensitivity Power Analyses for DM and HRT gives the initial sensitivity analyses of the effect of recruitment delays and changes in the age distribution on the power for the primary endpoints of DM and HRT that were presented previously. For DM we examined a recruitment delay that would result in the average follow-up time being reduced by four months. For HRT we chose an average reduction of follow-up to be six months. We looked at the effect of an age distribution of 15:23:45:17 for the age categories 50-54, 55-59, 60-69, 70-79. We have also calculated the combined effects of recruitment lags and changes to the age distribution though not accounting for the longer lags in accruing the older ages.

The power for cancer endpoints is more sensitive to reductions in average follow-up than the power for CHD. This is attributable to our design assumption that the lag time to full-preventive effects for cancer is linear over ten years, whereas CHD effects reach their maximum level after three years. Thus reductions in follow-up for cancer reduces the opportunity to observe the maximum treatment differences. The power for CHD is more sensitive to the age distribution of the recruited population, owing to the stronger dependence of CHD rates on age.

For the most part, either of the deviations examined has only a modest effect on power (2% - 3% reduction); combined, the effects are more concerning, particularly for the ERT and CHD hypothesis. These analyses have guided the development of our recruitment monitoring plan. This process will require diligent supervision and continued effort on the part of CCs, however, to avoid any further losses.

Additional sensitivity analyses examining recruitment delays in CaD and adherence factors for all three clinical trial components are underway and will be presented at the December 1996 meeting of the DSMB.

Table 11.1

Design Assumptions and Current Estimates

Design Assumptions	Monitoring Parameter	Design Value	Current Estimate for HRT	DM	CaD
Uniform Accrual Rate	Average follow-up	8.92 yrs. 7.92 yrs for CaD	8.37[1]	8.59[1]	6.87[1]
Baseline Characteristics	% randomized as				
Age	50-54	10%	19%	21%	20%
	55-59	20%	23%	26%	25%
	60-69	45%	41%	40%	41%
	70-79	25%	18%	14%	14%
Hysterectomy Status	Intact Uterus	55%	60%		
	Hysterectomized	45%	40%		
Loss to Follow-up/ Competing Risk	Event rate (%/year) CHD	2%	no data available		
	All others	3%			
Outcomes	Incidence Rates among Control Group				
Breast Cancer	(%/year)	0.355%[2]	no data available		
Colon Cancer		0.160%[2]			
CHD		0.294%[2]			
Hip Fractures		0.258%[2]			

[55] Assumes monthly goals will be met in all remaining months and that all current deficits will be filled by redefining the end of recruitment and extending HRT recruitment for VCCs without enhanced recruitment by 6 months.

[2] These values represent the expected incidence among control women during the early years of the study. Aging effects and secular trends are incorporated in the design, as appropriate.

Table 11.1. (continued)

Design Assumption and Current Estimates

Adherence DM Intervention	Parameter % cal from fat	Design Value Intervention	 Control	Current Estimate for Intervention	 Control
	Baseline	38	38	34.4[3]	34.4[3]
	Year 01	21.7	37.8	23.1[4]	34.0[5]
	Year 02	22.6	37.2	25.5[6]	34.9[7]
	Year 10	26	34		
HRT	% stopping intervention				
	Year 1	6%		9.5%	
	Years 2-10	3%/year		No data available.	
CaD	% stopping intervention				
	Year 1	6%		13.4%[8]	
	Years 2-9	3%/year		No data available.	

[3] Based on 1006 baseline *Four Day Food Records* (380 Intervention, 626 Control) and 5882 Year 1 Control group FFQ's (see *Table 6.5*).

[4] Based on 172 Year 1 *Four Day Food Records* and 4040 Year 1 *FFQs* in the Intervention Arm.

[5] Based on 277 Year 1 *Four Day Food Records* and 5882 Year 1 *FFQs* in the Control Arm.

[6] Based on 356 Year 2 FFQs in the Intervention Arm

[7] Based on 545 Year 2 FFQs in the Control Arm

[8] Calculated as annualized rates using data from *Table 4.3 - Intervention Status*

Table 11.2

Sensitivity Power Analyses for DM and HRT

Dietary Modification and Breast Cancer

		Power (%)			
Year	Intervention Effect (%)	Design	Average follow-up reduced by 4 months	Change in Age Distribution*	Change in Age Dist. AND average follow-up reduced by 4 months
2001	11	29	27	29	26
	12	37	33	36	33
	14	45	41	44	40
2004	11	65	61	64	60
	12	77	73	775	72
	14	**87**	**84**	**86**	**83**

Dietary Modification and Colorectal Cancer

		Power (%)			
Year	Intervention Effect (%)	Design	Average follow-up reduced by 4 months	Change in Age Distribution*	Change in Age Dist. AND average follow-up reduced by 4 months
2001	18	39	35	36	33
	20	47	43	43	39
	22	55	50	51	46
2004	18	84	81	81	77
	20	**91**	**89**	**89**	**86**
	22	96	94	94	92

*Age distribution for the design is 10:20:45:25 for age categories 50-54, 55-59, 60-69, 70-79. Alternative distribution is 15:23:45:17.

Table 11.2 (continued)

Sensitivity Power Analyses for DM and HRT

ERT and CHD

		Power (%)			
Year	Intervention Effect (%)	Design	Average follow-up reduced by 6 months	Change in Age Distribution*	Change in Age Dist. AND average follow-up reduced by 6 months
2001	25	46	41	40	35
	30	62	56	54	49
	35	76	70	68	62
2004	25	64	62	57	55
	30	**81**	**79**	**74**	**71**
	35	92	90	87	85

PERT and CHD

		Power (%)			
Year	Intervention Effect (%)	Design	Average follow-up reduced by 6 months	Change in Age Distribution*	Change in Age Dist. AND average follow-up reduced by 6 months
2001	25	54	48	47	42
	30	70	64	62	57
	35	84	79	77	71
2004	25	73	71	65	63
	30	**88**	**86**	**82**	**80**
	35	96	95	92	91

*Age distribution for the design is 10:20:45:25 for age categories 50-54, 55-59, 60-69, 70-79. Alternative distribution is 15:23:45:17.

12. 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 12.1
Publications

Name of Manuscript	Writing Group	Data Focus	Type	Stage	Publisher
Informed consent in the Women's Health Initiative Clinical Trial and Observational Study	**McTiernan**, Franzi, Johnson, Manson, Nevitt, Rossouw, Taylor, Carleton	Gen.	2	10	Journal of Women's Health, Vol 4, Num.5
Low-fat diet practices of older women: Prevalence and implication for dietary assessment"	**Patterson**, Caggiula, Coates, Kristal, Ritenbaugh, Snetselaar, Stern, Tylavsky, Van Horn	Gen.	2	10	Journal of the American Dietetic Association, Vol 96, 670-679, 1996
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	2	10	Menopause, Vol 3, No. 2, pp. 71-76 1996
The evolution of the Women's Health Initiative: Perspectives from the NIH"	**Rossouw**, Finnegan, McGowan, Clifford	Gen.	2	10	Association, Vol. 50, 50-55, 1995
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.	2	10	Nutrition & Women's Health, Chapter 18, 510-542, 1996
Women Health Initiative: Why now? What is it? What's new?	**Matthews**, Shumaker, Hunt, Bowen, Klesges, Kaplan, Ritenbaugh, Langer, Weiss	Gen.	2	9	American Psychlogist
A comprehensive data management system for multicenter studies	**Anderson**, Davis, Koch	Gen.	2	8	Controlled Clinical Trials
The effects of ethnicity on mammography utilization in a postmenopausal population	**Bush,** Langer	Gen.	3	8	

Name of Manuscript	Writing Group	Data Focus	Type	Stage	Publisher
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	2	8	Controlled Clinical Trials
WHI design manuscript	**Prentice**, Rossouw, Furberg, Johnson, Henderson, Cummings, Manson, Freedman, Oberman, Kuller	Gen.	2	8	Controlled Clinical Trials
Combined hormone replacement therapy and occurrence of disease in postmenopausal women	**Johnson**, McTiernan, Bachman, Beresford, Dunn, Grady, Judd, Hunninghake, Manson	Gen.	2	5	
Statistical methods adjusting for restricted population and measurement error	**Wang**, Anderson, Prentice	Gen.	2	5	
Factors associated with insurance status among participants in the WHI	**Hsia**, Sofaer, Lillington, Zapaka, Limacher, Kiefe, Sennott-Miller, Mason, Bowen, Kemper	Gen.	2	3	
Correlates of endogenous sex hormone concentrations in WHI	**McTiernan**, Wactawski-Wende, Chen, Meilahn, LaVelleur, Cummings, Hiatt, Baum, Hulka, Wang	CT	2	3	
Psychosocial and behavioral correlates of moderate alcohol consumption in women	**Powell**, Hymowitz, Criqui, Ockene, Finnegan, Castro, Trevisan, Curb, Hunt, Noonan	CT	2	3	
Patterns of antihypertensive treatment and control among postmenopausal women	**Wassertheil-Smoller**, Manson, Wong, Lasser, Kotchen, Langer, Grimm, Black, Psaty, Anderson	OS	2	3	
Cardiovascular and other physiological correlates of depression	**Wassertheil-Smoller**, Talavera, Campbell, Shumaker, Ockene, Robbins, Dunbar, Greenland, Cochrane	Gen.	2	3	
Prevalence of pelvic organ prolapse and urinary incontinence in women	**Clark**, Nygaard, Harris, Varner, Chang, Hendrix, Barnabei, Maddox, McTiernan	CT	2	2	

Name of Manuscript	Writing Group	Data Focus	Type	Stage	Publisher
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.	2	2	
Body weight and anthropometric measures of adiposity	**Manson,** Kotchen, Perri, Lewis, Johnson, Freed, Hall, Allen, Foreyt, Tinker, Noonan, Stefanick	OS	2	2	
The relationship of dietary phytoestrogens menopausal to symptoms and major morbidity in postmenopausal women	**Roman**, Woods, Caggiula, Judd, Brzyski, Liu, Burke, Assaf, Patterson	CT	2	2	
Are antioxidants associated with bone mineral density in older women?	**Seeley**, Kritchevsky, Wactawski-Wende, Csuka, Haan, Cauley, Jackson, Caan, LaCriox, Wang	CT	2	2	
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.	2	2	
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	2	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 12.2
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? (Y/N)
AS1	ADAPT	John Crouse	Greg Burke	Approved	NA	dropped		5 CCs	DM	4,000	NA	NA	5 years	NA	NA	NA
AS2	PLCO-OS	Joel Weissfeld	Lew Kuller	Not an AS	NA	pending submission		1 CC	OS	2,200	NA	NA	WHI	NA	NA	NA
AS3	PLCO-Partners	Joel Weissfeld	Lew Kuller	Not an AS	NA	dropped		1 CC	WHI Partners	NA	NA	NA	NA	NA	NA	NA
AS4	Prostate Cancer-Partners	Al Oberman James Shikany	Al Oberman	Approved	yes	pending submission		ALL	DM Partners	10,922	NA	4/1/96	5 years			YES
AS5	Fat Distaste	Pamela Green	Deb Bowen	Approved	NA	funded	yes	none	DM	160	NA	4/1/95	1.5 years	NA	NA	
AS6	Arthritis	Susan Hughes	Phil Greenland	Approved	NA	dropped		none	OS	1,200	NA	1/1/96	5 years	NA	NA	YES
AS7	Ankle/Arm BPI	Lewis Kuller	Lew Kuller	Approved	NA	under review		12, 14, 16, 22, 24, 25, 45	HRT	6,500	NA	asap	9 years		NO	
AS8	Partner's Health Study	Robert Langer	Robert Langer	Approved	NA	pending submission		none	WHI Partners	1,500	NA	7/1/94	15 mos.			
AS9	Oral Bone Loss	Cora E. Lewis	Al Oberman	Approved	NA	funded	yes	none	OS	650	NA	7/1/95	7 years	YES	YES	YES
AS10	Urine Metabolites	Elaine Meilahn	Lew Kuller	Approved	yes	dropped		All	DM	80,000	NA	7/1/95	5 years	NO	NO	YES
AS11	Sleep and Mood Predictors	Daniel Kripke	Robert Langer	Approved	NA	funded	yes	none	OS	600	urine	8/1/95	5 years	NA	NA	
AS12	Empowerment	Charles Mouton	Norm Lasser	Declined	NA	pending submission		1 CC	DM only	360	NA	7/1/94	4 years	NA	NA	NA
AS13	Spinal Stenosis	Lewis Kuller	Lew Kuller	Approved	NA	funded	yes	none	CT	150	NA	ASAP	12 years	NO	NO	
AS14	HDL Metabolism	Scott Going, Tamsen Bassford	Tom Moon	Approved	NA	funded	yes	none	OS	200	NA	7/1/94	2 years	YES	YES	NO
AS15	Osteopenia	Jean Wactawski-Wende	Maurizio Trevisan	Approved	yes	funded	yes	none	OS	1,300	NA	NA	4 years			
AS16	LEAD & BPI	Mary McDermott	Phil Greenland	Approved	NA	dropped		7 CCs	OS, 65+	5,500	NA	7/1/95	5 years	NA	NA	
AS17	Domestic Violence	Charles Mouton	Norm Lasser	Approved	yes	pending submission		none	OS	1,000	NA	10/25/94	2 years			
AS18	Fat Aversion	Jim Grizzle	Deb Bowen	Approved	yes	under review		Birmingham, Atlanta, Miami	WHT women	120	NA	11/1/95	4 years			
AS19	Coagulation Proteins	Anthony Orencia	Phil Greenland	Approved	NA	dropped		Iowa, LaJolla, Chiago w.side	OS	782	1.2 ml	NA	4 years	NA	NA	

Table 12.2 (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? (Y/N)
AS20	EBCT-1 (Coronary Screening)	Robert Detrano	Rowan Chlebowski Harbor UCLA	Approved	NA	dropped		Irvine	OS	2,666	NA	2/1/96	2 years	NA	NA	YES
AS21	EBCT-2 (Effect of DM, HRT, CaD)	Robert Detrano	Rowan Chlebowski Harbor UCLA	Approved	NA	dropped		2 CCs	CT	2,666	NA	NA	5 years	NA	NA	YES
AS22	Vascular Compliance	Jennifer Robinson	Richard Grimm	Approved	NA	dropped		none	CT	500	NA	NA	9 years			
AS23	NSAIDS	Randall Harris	Rebecca Jackson	Not an AS	NA	Not an AS		All	OS	100,000	NA	NA	8 years			
AS24	Skeletal Health	Diane Schneider	Robert Langer	Approved	yes	under review		none	OS	168	NA	1/3/95	2 years			
AS25	Ankle-Arm BPI	Kamal Masaki	David Curb	Approved	yes	under review		none	OS	2,700	NA	7/1/95	2 years			YES
AS26	Knee-Hip OA	James Cerhan	Robert Wallace	Approved	yes	under review		ALL	HRT	11,374	NA	4/1/96	5 years			YES
AS27	Vitamin D, Calcium, & Breast Cancer	Barbara Hulka	David Sheps	Approved	yes	under review		ALL	CaD/OS	2,600	2 ml	6/1/96	5 years			YES
AS28	Aging	S. Wassertheil-Smoller	S. Wassertheil-Smoller	Approved	yes	pending submission		none	NYC OS ppts.	NA	1.5 ml	NA	5 year follow-up	NO	NO	NO
AS29	Oxidation Status	Michael Gaziano JoAnn Manson	JoAnn Manson	Approved	yes	under review		none	HRT	300	NA	9/1/95	6 months			
AS30	Lung Cancer	Geoffrey Kabat	S. Wassertheil-Smoller	Approved	yes	pending submission		ALL	OS	67,000	2.5 ml	6/1/96	4 years			YES
AS31	Eye Care Use	Robert Kleinstein	Al Oberman	Approved	yes	funded		none	OS	300	NA	NA		YES	YES	NO
AS32	Recruitment Tech.	Kathryn Boe	Robert Langer	Approved		under review		none	NA	400	NA	NA		NO	NO	NO
AS33	HRT and Body Fat	Charlotte Mayo	Al Oberman	Approved	yes	funded	yes	none	OS	690	NA	7/31/95	6-8 months	YES	YES	NO
AS34	Bone Morphology	Dorothy Nelson	Susan Hendrix	Approved	yes	under review		none	CT	400	NA	5/1/96	4 years			
AS35	Risk Factors for Fatigue	Arthur Hartz	Jane Kotchen	Approved	yes	under review		Iowa	NA	3,000	NA	7/1/96	4 years			possible
AS36	HRT and Mammographic Density	Barbara Hulka	David Sheps	Approved	yes	under review		ALL	HRT	NA	NA					YES
AS37	Lipid Markers	JoAnn Manson	JoAnn Manson	Decision Pending	NA	pending submission		Brimingham , Buffalo, LaJolla	NA	NA	NA	9/1/96	NA			
AS38	Hemostatis	Paul Ridker	JoAnn Manson	Decision Pending	NA	pending submission		Brimingham , Buffalo, LaJolla	NA	NA	NA	9/1/96	NA			
AS39	WHI Memory Study	Sally Shumaker	Curt Furberg	Approved	yes	funded	yes	ALL except Seattle	HRT women	4,800	NA	3/1/96	6 years	YES	YES	YES

Table 12.2 (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? (Y/N)
AS40	Mammography Behavior	S. Wassertheil-Smoller	Sylvia Wassertheil-Smoller	Approved	yes	pending submission	yes	none	NYC ppts.	All	NA	NA	NA	NO	NO	NO
AS41	Metab. Lipoproteins	Joel Morrisett	John Foreyt	Declined	NA	pending submission		none	Houston ppts.	24	blood	10/1/95	5 years		NA	NO
AS42	Insurance	Judith Hsia Shoshanna Sofaer	Vallery Miller	Declined	NA	pending submission		ALL	OS	All	NA	NA		NO	NO	NO
AS43	Bone Mass	William Goodman	Howard Judd	Declined	NA	pending submission		none	Los Angeles CT	362	blood, urine	10/1/95	4 years	NO	NO	NO
AS44	Vaginal pH	Anthony Schaeffer	Philip Greenland	Approved	yes	funded	yes	none	HRT ppts.	100	vaginal fluid	asap	NA	YES	YES	PC
AS45	RSBD Self-Report in the WHI	James R. Herbert	Langer/Lo	Approved	yes	pending submission		14, 16, 21, 30, 48, 49, 50, 53, 65, 67,	WHI Women	1,350	NA	8/1/96	2 years			PC
AS46	Prostate & Colorectal Cancer	Albert Oberman	Yasmin Rahmani	Approved	yes	pending submission		All	DM Husbands	34,200	NA	12/1/96	5 years			ues
AS47	Diet & Motivation	Langer/Lo	RossPrentice	Approved	yes	funded	yes	none	DM		NA			YES	YES	NO
AS48	Prostate cancer pilot	Sylvia Smoller	John Foreyt	Approved	yes	funded	yes	none	DM, HRT, OS	1,607	NA	2/1/96	5 / Mo.	YES	YES	
AS49	ADA- PILOT	Yasmin Rahmani	A. McTiernan	Declined	NA	pending submission		none	DM		NA		NA	NA	NA	
AS50	ADA- PILOT	BethBurrows	Sylvia Smoller	Approved	yes	pending submission		none					1 yr			NO
AS51	Bone Quality in OS	Adrian LeBlanc		Declined	NA	pending submission		none	OS	400				NA	NA	NA
AS52	Endogenous Sex Hormones	Anne McTiernan		Approved	yes	pending submission		All	OS	782	2ml	2/1/97	4 years			
AS53	Diet & Hormone Dev.	Geoffrey Kabat		Declined	NA	pending submission		20	OS	17,500	blood, urine	4/1/97	4 years	NA	NA	NA
AS54	Women & Minority Recruitment	Albert Oberman		Declined	NA	pending submission		none	DM	400	N/A	10/1/96	4 years			
AS55	Predictors of Participation among Latinos	Gregory Talavera		Approved	yes	pending submission		4	DM, HRT, OS	17,270	N/A	9/1/96	4 years			YES
AS56	Behavioral & Psychosocial Predictors	Alice Thomson		Approved	yes	pending submission		none	DM	260	N/A	9/1/96	2 years			NO
AS57	Hispanic Women's Advocacy and Reten. Strategies	Cheryl Kitenbaugh		Approved	yes	under review		none	OS	120	N/A	9/1/96	2 years			NO

Table 12.2 (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? (Y/N)
AS58	Enrollment of Hispanic Women in Prevent. Trials	Marianna Baum		Approved	yes	pending submission		none		120	N/A	9/1/96	3 years			NO
AS59	Prevalence of thyroid problems	Marianna Baum		Declined	NA	pending submission										
AS 60	Diet and prostate CA in WHI spouses	Al Oberman		Approved	yes	pending submission										
AS 61	Memory in HRT in WHIMS participants	Robbins		Approved	yes	pending submission										
AS 62	Age Related Maculopathy			Approved	yes	pending submission			HRT	3,000			9 years			
AS 63	Eating Style Index	Pam Haines		Approved	yes	pending submission			OS	800		9/30/06	2 years		YES	
AS 64	Mammography Sensitivity			Declined		pending submission				600			3 years			