Women's Health Initiative
Clinical Trial and Observational Study

Annual Report

Volume 1: Study Progress
September 1, 1993 to August 31, 1994

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Executive Summary

The Women's Health Initiative Clinical Trial and Observational Study was launched into the field on September 1, 1993. Recruitment into the Hormone Replacement Therapy (HRT) component and the Dietary Modification (DM) component of the Clinical Trial is underway with 4,496 women currently randomized, 1,447 to HRT (59.6% of cumulative goal) and 3,665 to DM (78.7% of cumulative goal). Recruitment into the Calcium and Vitamin D (CaD) component is scheduled to begin at the first annual follow-up. Enrollment into the OS, delayed by the need to obtain OMB approval, was officially opened on September 1, 1994.

The lag in recruitment to HRT and DM is related to both some initial delays in Clinical Center startup and in the size and complexity of the program. A major streamlining effort was undertaken to make the program fit within the existing budget. Since that time good progress has been made in meeting monthly goals. Continued effort will be needed to meet the cumulative goals. Attention is also needed to meet subgroup goals for age, hysterectomy status, and minority populations.

With the minimal follow-up data currently available, the adherence to HRT cannot yet be accurately estimated. Intervention activities for DM are proceeding with 70 intervention groups formed and excellent completion of sessions and self-monitoring reports of fat consumption. The major issues in DM are the delays in assigning women to intervention groups and, for clinic operation, the size of the groups.

Quality assurance issues, such as timeliness and completeness of data, have achieved a satisfactory level. Variation between sites should be further monitored for clarification of existing problems and further improvements.

Further development of follow-up and outcomes procedures is underway. The existing data are limited but are included in this report for completeness. More detail will be provided in the future. Activities of the CaD and OS components will also be monitored over the coming year.

1. Preliminary Remarks

This report documents study activities of the Women's Health Initiative Clinical Trial (CT) and Observational Study (OS) during the period September 1, 1993 to August 31, 1994. Volume 1: Study Progress summarizes enrollment, follow-up, intervention, outcomes, and data quality issues. Study-wide and Clinical Center (CC) specific performance reports are included. Volume 2: Clinical Trial Monitoring compares randomization groups for each CT component (Hormone Replacement Therapy (HRT), Dietary Modification (DM), and Calcium and Vitamin D [CaD]) with respect to follow-up, safety and outcomes. Volume 1 is intended for review and reference by all WHI centers, committees and investigators. To protect the blinding and confidentiality of results, Volume 2 is distributed to the WHI Data and Safety Monitoring Board (DSMB) and appropriate National Institutes of Health (NIH) and Clinical Coordinating Center (CCC) staff.

All reports summarize data provided to the CCC by August 31, 1994. Except for *Table 2.1. - Cumulative Recruitment Activity Summary* describing recruitment strategies by CC, 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:

- Ogden BioServices, Rockville, Maryland, CCC subcontractor for specimen repository and drug distribution (Harrison Hoppes, PhD, President).
- Epicore, 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).

Table 1.1.
Database Abbreviations for WHI CCs

Abbreviation	CC Institution and Location	Principal Investigator
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
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 MPH
CHICAGO	Northwestern University Chicago and Evanston, Illinois	Phillip 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	Thomas Moon, PhD
UCDAVIS	University of California, Davis Sacramento, California	John Robbins, MD

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 Hormone Replacement Therapy (HRT) or Dietary Modification (DM) components are invited to Screening Visit 1 (SV1). For efficiency, many CCs ask women to complete *Form 60 - Food Frequency Questionnaire* (FFQ) to determine dietary eligibility prior to scheduling SV1.

Women attending SV1 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 SV1 or through mail contact immediately thereafter. Women still eligible for HRT or DM are given component-specific informed consent documents and are scheduled for Screening 2.

Women attending SV2 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 (SV3) 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 receive appropriate laboratory results.

At SV3, 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. Women are randomized to HRT, DM, or both, as appropriate, at this visit.

Women who become ineligible for or uninterested 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 Calcium and Vitamin D component (CaD) are invited to participate 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 more variable between 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.

Note also that the WHILMA data collected before SV1 is labeled as SV0, regardless of the format of data collection (visit, mail, or telephone contact).

2.2. Recruitment

Recruitment efforts of CCs are tailored to the local population and resources. *Table 2.1. - Cumulative Recruitment Activity Summary* summarizes the types and volumes of various activities conducted by each CC between September 1, 1993 and August 31, 1994. The initial NIH announcement of Vanguard Clinical Center (VCCs) on March 8, 1993 generated considerable interest. Most VCCs collected up to 3,000 names of interested women. Initial screening efforts focused on these enriched lists that were not exhausted until the spring of 1994. The experience documented in this report thus represents the results of recruitment efforts primarily directed at highly motivated women.

2.3. Screening

Screening for the CT components officially opened in VCCs on September 1, 1993. Ten VCCs began screening participants by the end of September. Local IRB issues, facilities and staffing delays, and competing study recruitment delayed the start of screening activities at several sites until October (four VCCs) and November (two VCCs).

Figure 2.1. - Projected and Actual Screening Visits displays cumulative study-wide screening activities by month with the projected number required based on current yield information. The first four months of recruitment showed activities well below the initially projected required number but considerable effort has been made to overcome the initial shortfall. To date, the study has conducted 12,858 SV1s, 7,017 SV2s, and 5,072 SV3s. It was noted early on that screening and data collection activities as originally implemented were too onerous. In November 1993, a Recruitment and Screening Task Force was formed and asked to make recommendations to improve the efficiency of the program, particularly regarding screening and eligibility. The most important change increased the efficiency of early screening activities, primarily by identifying more of CT ineligible women before SV1, thereby reducing the number of SV1s required. These changes were implemented in the first quarter of 1994.

Original projections assumed that 34% of SV1 women would proceed to SV2, 96% of SV2 women would proceed to SV3, and 98% of SV3 women would be randomized. From these and an average time of one month between screening visits, we calculated that, to meet VCC recruitment goals by August 31, 1996, the following level of screening activities should be maintained beginning by dates indicated: 131 SV1s per month as of October 1993; 45 SV2s per month as of November 1993; and 43 SV3s per month as of December 1993.

Current data suggest that these initial projections were inaccurate, especially with recruitment tailored for CT alone. Yields by stage during this reporting period (shown in *Table 2.2. - Recruitment Yield by Stage*) were as follows:

	Yield Estimates		Projected # of Monthly Visits/CC		
Stage	Initial	Current	Initial	Current CT only	Current CT + OS
SV1	34%	81%	131	62	108
SV2	96%	94%	45	50	50
SV3	98%	91%	43	47	47

This suggests that 69% of women attending SV1s are eventually randomized, more than twice the original estimate of 33%. *Table 2.3. - Clinical Center Specific Recruitment Yields* summarizes the VCC-specific yields by stage. We also note that across all VCCs, the yield of SV0 is approximately 71%. For VCCs regularly entering all prescreening data, the SV0 yield is approximately 62%.

Table 2.4. - Race and Ethnicity Specific Recruitment Yields by Stage and *Table 2.5. - Age Specific Recruitment Yields by Stage* present summaries of yields for CT randomizations by race/ethnicity and age category. Though there are few women currently randomized in some racial/ethnic categories, we note that the estimated cumulative yield from SV1 varies from 61% among Asian/Pacific Islanders to 71% among Native Americans. Among those categories with adequate numbers to provide stable estimates, however, the cumulative yields range only from 66% to 69%. Yields from SV0 are more variable but it is not possible to determine whether this is actually variation in eligibility and willingness to participate or an artifact of the missing data on ineligibles that varies greatly by CC and hence by race/ethnicity. There is some evidence of a lower yield in older women; among women over the age of 70 attending SV1, 65% would be randomized whereas among women younger than 70, the yield is estimated to be near 70%. A similar trend is seen in the SV0 yields.

Using these yield estimates, the projected number of visits required for CT enrollment alone in a steady state recruitment period of 36 months would be: 62 SV1s per month beginning in the second month of recruitment; 50 SV2s per month beginning in the third month of recruitment; and 47 SV3s per month beginning in the fourth month of recruitment. Compared to these revised projections, the overall study performance for screening during the period September 1, 1993 to August 31, 1994 is: SV1-112%; SV2-87.7%, and SV3-74.9%.

The expected number of OS enrollments from this plan would be 603 per CC (18 per month over 33 months, assuming 95% of CT ineligibles enroll in OS). To achieve the OS goal of 2,200 participants per CC in 36 months, each CC needs to enroll 62 OS participants per month. The number of SV1s needed for joint CT and OS recruitment is approximately 108 per month (again assuming a 95% enrollment rate of OS eligible women).

Individual VCC performance is summarized in *Tables 2.6.* through *2.9. - Clinical Center Ranking by Screening Visit Count* (SV0--SV3). These reports show the ranking of CCs by total number of screening visits conducted within each type (SV0, SV1, SV2, SV3). Since most women who are ineligible for CT are identified at SV0 and data from these women are often not entered, the number of women contacted for SV0 activities is thought to be

substantially underestimated by this report. The values shown here should be interpreted as lower bounds on the number of women undergoing prescreening activities. The level of SV1, SV2 and SV3 activities are shown both to rank VCCs and to compare their cumulative activity with that projected from revised yield estimates.

There is considerable variability in the number of screening activities conducted among VCCs. The variability in the number of SV1s is especially large, reflecting a combination of startup delays, variation in CT eligibility, and data entry practices. Using the revised projections calculated above for CT recruitment only, 12 VCCs would surpass the cumulative SV1 goal of 682, two VCCs would surpass the cumulative SV2 goal of 500, and three VCCs would have 90% or more of the SV3 goal of 423.

2.4. Randomization and Enrollment

Figure 2.2. - Projected and Actual HRT and DM Randomizations shows the projected and actual number of women randomized into HRT and DM by month. As noted in the screening activities, the first four months of study operations showed much less activity than expected. Not until March, 1994, were significant numbers of women randomized at most sites. Since that time, however, considerable progress has been made to meet the accrual goals.

Table 2.10. - Randomization Activity by Study Component and Month shows that 1,447 women have been randomized to HRT. This represents 60% of the cumulative study-wide goal. In the most recent month of recruitment (August 1994) 260 women were randomized (97% of monthly goal). To meet cumulative goals for HRT within six months (by March, 1995), VCCs must randomize an average of 433 women (27 per VCC) per month or 160% of the monthly goal. A randomization rate of 130% of goal would result in our meeting cumulative VCC goals by September 1995.

Randomizations into DM are 3,665 women (79% of the cumulative goal to date). In August, the total number randomized was 646 or 125% of the study-wide monthly goal. With an average monthly recruitment of 132% of monthly goal (686 for all VCCs or 43 per VCC per month), the cumulative goal for DM would be reached in six months. At the average randomization rate observed over the last four months (616/month) we would reach cumulative goals by July 1995 (10 months).

The number of women currently participating in both HRT and DM is 616 or 13.7% of the total CT enrollment of 4,496 women. The CT sample size estimates of 63,000 assume an overlap of 15.8%. This lower than projected overlap probably results from the lag in HRT randomizations.

Table 2.11. - Clinical Center Randomization Activity shows the cumulative and most recent month's randomizations into each study component by CC, with CC ranking by the total number of women randomized. One VCC (Iowa) has randomized 162 women into HRT, achieving 107% of their cumulative goal. In August, five VCCs randomized more than 100% of their monthly HRT goal. Fourteen VCCs randomized more than 100% of their monthly DM goal in August and two VCCs (Minneapolis and Seattle) have randomized 107% of their cumulative DM goals; these same CCs have exceeded their monthly goals for six consecutive months.

We note considerable variation among VCCs in the overlap between CT components (from 7% to 25%).

Since no CT participant has yet reached the time for her annual visit, there have been no randomizations to CaD. It is expected that CaD medications will be available in December 1994. Randomizations into CaD should begin at that time.

No women have been enrolled into OS pending OMB and IRB approvals.

2.5. Exclusions

Available data on reasons for CT exclusions can be given only a loose interpretation because of missing data on ineligibles.

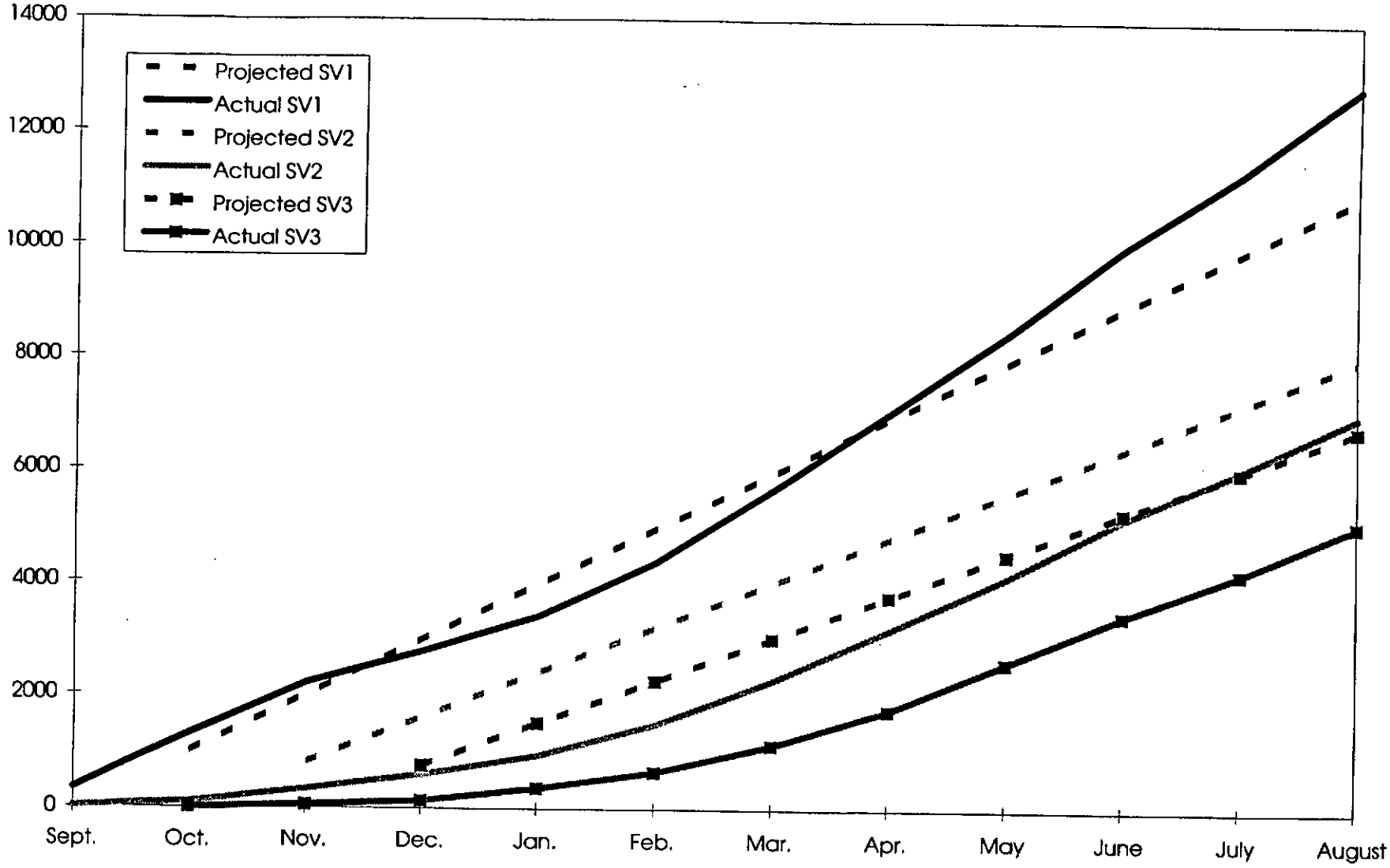
During the prescreening activities of SV0, the primary reason for exclusion for HRT is lack of interest. For HRT, the most prevalent exclusion criteria are those related to interest in HRT willingness to be randomized. During the Eligibility Screen (*Form 2/3*) conducted at SV0, only 27% of women indicated that they are interested in the hormone study. Among women with uteri (59%), 26% were interested, and among women currently on hormones (40%), 24% were interested. Interest is higher in minority women (41% in Hispanic and 31% in African/American) than in Whites (26%). The primary reason for excluding women from DM prior to SV1 is dietary fat intake. Using the cutpoint of 32%, approximately 50% of women are being excluded from DM.

For women attending an SV1, the primary exclusion is based on lack of interest (consent). *Table 2.12. - Reasons for Refusing/Revoking Consent by Study Component* 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. Overall, 85% of women asked to sign the screening consent have agreed to do so; 37% of women offered HRT participation and 82% of women offered DM participation have signed the component-specific consents.

Among those women who attend a clinic visit but do not consent to screening procedures, commonly reported reasons for not participating include: study limitations (wanting to participate in one or more of the active interventions, 12.8%); personal issues (12.9%); and study contacts and travel issues (over 9% each). For HRT the primary reason was study limitations (34.6%), with worries about symptoms, procedures or risks (18.6%), and "other" (21%) representing a large proportion of the stated reasons. For DM, required study contacts, personal issues, other, and no stated reason given by 18%, 16%, 25% and 15% of the women, respectively.

Figure 2.1

Projected and Actual Screening Visits

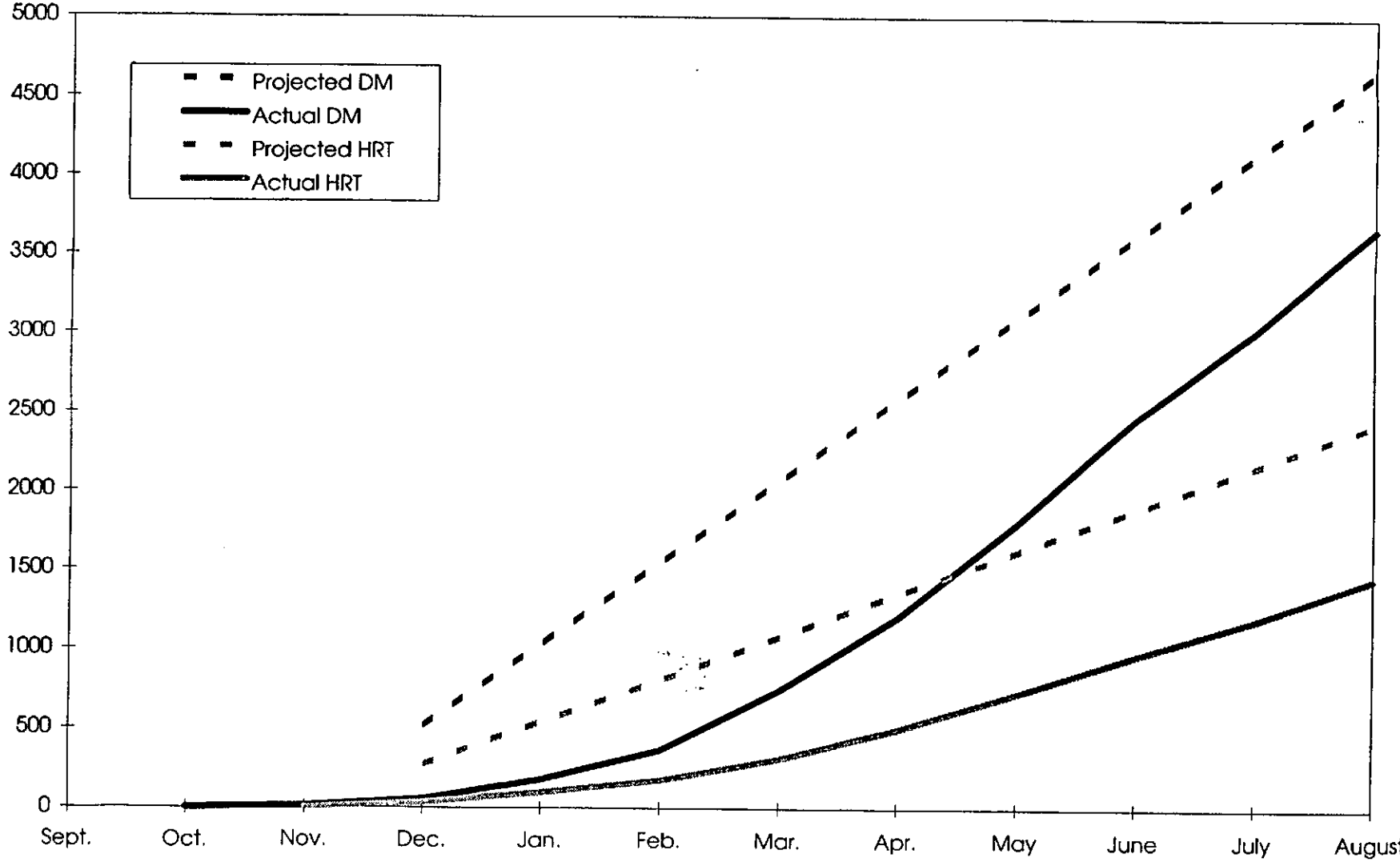


Data as of August 31, 1994

KMC2.XLS

Figure 2.2

Projected and Actual HRT and DM Randomizations



Data as of August 31, 1994

KMC1.XLS

Table 2.1
Cumulative Recruitment Activity Summary
Date: September 1, 1993 - August 30, 1994

				New Articles or Reports			Public Service Announcements			Presentations			
		Letters & Brochures	Repeat Letters & Brochures	In Print Media	On TV	On Radio	In Print Media	On TV*	On Radio*	To Older Women	To MDs & Health Profes-sionals	To Other	Other Sources
Vanguard Clinical Centers													
University of Alabama	# of Events	126685	2000	6	6	3	0	0	2	27	3	6	
Birmingham	# of Responses	2716	0	197	62	15	0	0	14	210	17	0	0
University of Arizona	# of Events	34625	1876	50	34	24	1	2	1	115	25	66	
Tucson/Phoenix	# of Responses	1536	178	1058	335	48	8	2	0	220	27	204	573
Bowman Gray School of Med.	# of Events	22345	850	7	4	2	0	1	0	5	9	2	
Winston-Salem	# of Responses	1460	400	1031	300	4	0	50	0	18	0	0	90
Brigham and Women's Hosp.	# of Events	18263	0	14	3	19	0	0	2	2	40	1	
Boston	# of Responses	4180	0	0	0	0	0	0	0	0	0	0	125
University of California, Davis	# of Events	67343	370	19	4	1	6	0	0	14	8	4	
Davis	# of Responses	3648	155	242	94	0	119	0	0	55	0	4	0
Univ. of Calif., San Diego	# of Events	31789	49	13	12	9	1	1	5	50	23	10	
La Jolla/Chula Vista	# of Responses	1223	0	410	599	7	5	0	2	87	11	5	27
Emory Univ. School of Med.	# of Events	18950	0	8	7	0	0	0	0	59	3	2	
Atlanta	# of Responses	2855	0	272	237	0	0	0	0	167	1	7	0
F. Hutchinson Cancer Res. Ctr.	# of Events	45107	0	15	4	4	0	0	0	2	5	0	
Seattle	# of Responses	6121	0	75	0	0	0	0	0	0	0	0	10
University of Iowa	# of Events	68588	0	47	6	4	0	0	0	1	10	5	
Iowa City/Bettendorf	# of Responses	3859	0	220	0	0	0	0	0	0	0	0	0

Table 2.1
Cumulative Recruitment Activity Summary
Date: September 1, 1993 - August 30, 1994

		Letters & Brochures	Repeat Letters & Brochures	New Articles or Reports			Public Service Announcements			Presentations			Other Sources
				In Print Media	On TV	On Radio	In Print Media	On TV*	On Radio*	To Older Women	To MDs & Health Profes-sionals	To Other	
Vanguard Clinical Centers													
Univ. of Med. & Dent. of N.J.	# of Events	43061	6493	8	1	1	0	0	0	1	1	0	
Newark	# of Responses	761	0	219	3	7	0	0	0	2	0	0	0
Memorial Hospital of R. I.	# of Events	15880	0	53	21	12	0	8	0	28	11	19	
Pawtucket	# of Responses	1425	0	38	7	35	0	1	0	34	2	2	529
University of Minnesota	# of Events	17129	0	0	0	0	0	0	0	0	0	0	
Minneapolis	# of Responses	3194	0	0	0	0	0	0	0	0	0	0	0
State University of N.Y.	# of Events	63487	0	19	5	4	0	1	6	18	9	12	
Buffalo	# of Responses	1775	0	661	220	35	0	4	18	153	4	16	243
Northwestern University	# of Events	75218	300	10	3	2	0	4	4	7	9	7	
Chicago/Evanston	# of Responses	4466	0	0	134	0	0	0	0	43	6	6	810
University of Pittsburgh	# of Events	85921	11035	16	6	0	4	0	0	9	3	3	
Pittsburgh	# of Responses	2845	97	92	110	0	0	0	0	3	6	13	0
University of Tennessee	# of Events	64239	0	9	5	4	0	3	0	8	4	4	
Memphis	# of Responses	1948	0	95	41	13	2	5	2	0	0	0	81
GRAND TOTALS:	# of Events	798630	22973	294	121	89	12	20	20	346	163	141	
	# of Responses	44012	830	4610	2142	164	134	62	36	992	74	257	2488

Data as of 08/31/94

Table 2.2
Recruitment Yield by Stage

Stage	State	N	%	Cum Yield from SV0	Cum Yield from SV1	Number Required for Recruitment into CT only	Number Required for Recruitment into CT + OS
SV0	Entering Stage	27742	100.00%				
	Exclusions	8225	29.65%				
	Yield of Stage	19517	70.35%	70.35%			
	Pending [1]	9150	46.88%				
SV1	Entering Stage	12252	100.00%			62/month	**108/month**
	Exclusions	2357	19.24%				
	Yield of Stage	9895	80.76%	56.82%	80.76%		
	Pending	3099	31.32%				
SV2	Entering Stage	6786	100.00%			50/month	**50/month**
	Exclusions	382	5.63%				
	Yield of Stage	6404	94.37%	53.62%	76.22%		
	Pending	1491	23.28%				
SV3	Entering Stage	4935	100.00%			47/month	**47/month**
	Exclusions	152	3.08%				
	Yield of Stage	4783	96.92%	51.97%	73.87%		
	Pending	287	6.00%				
	Randomizations	4496	94.00%	48.85%	**69.44%**	43/month	**43/month**
	OS Enrollments						**62/month**

[1] Pending is defined as women still eligible based on current data who have not proceeded to next stage. Percent pending is percent of yield of stage.

Data as of 08/31/94

Table 2.3
Clinical Center Specific Recruitment Yields

Clinical Center	SV0		SV1	SV2	SV3	Randomized		Cumulative
	N	Yield	Yield	Yield	Yield	N	Yield	Yield of SV1
Atlanta	2221	61.28%	95.60%	96.76%	96.31%	206	98.56%	87.81%
Birmingham	2263	78.88%	89.88%	96.87%	98.99%	283	96.59%	83.25%
Bowman	982	87.23%	80.77%	91.76%	96.13%	277	92.95%	66.22%
Brigham	2135	66.18%	93.86%	97.38%	98.44%	312	98.73%	88.83%
Buffalo	1390	54.18%	91.73%	96.08%	98.26%	278	98.58%	85.37%
Chicago	1557	78.89%	74.52%	94.46%	94.78%	229	97.03%	64.74%
Iowa City	3477	45.75%	85.82%	89.21%	93.35%	305	98.71%	70.55%
LaJolla	1001	99.60%	100.00%	99.32%	100.00%	272	84.74%	84.16%
Memphis	1419	91.25%	89.05%	98.33%	99.20%	338	91.11%	79.14%
Minneapolis	2299	79.59%	70.91%	91.33%	95.19%	372	98.94%	60.99%
Newark	815	99.75%	44.61%	93.39%	96.59%	196	69.26%	27.87%
Pawtucket	1091	60.55%	92.49%	92.54%	95.25%	330	96.77%	78.89%
Pittsburgh	777	99.35%	77.79%	94.11%	96.78%	280	93.02%	65.91%
Seattle	2762	52.77%	76.69%	95.46%	95.60%	359	97.29%	68.09%
Tucson	1528	76.79%	76.65%	82.54%	96.97%	180	93.75%	57.52%
UCDavis	2115	75.64%	87.33%	98.49%	99.31%	279	97.55%	83.33%

Data as of 08/31/94

Table 2.4
Race and Ethnicity Specific Recruitment Yields by Stage

		Native American				Asian/Pacific Islander				Black/African Americans			
				Cum Yield from				Cum Yield from				Cum Yield from	
Stage	State	N	%	SV0	SV1	N	%	SV0	SV1	N	%	SV0	SV1
SV0	Entering Stage	97	100.00%			210	100.00%			2007	100.00%		
	Exclusions	30	30.93%			57	27.14%			370	18.44%		
	Yield of Stage	67	69.07%	69.07%		153	72.86%	72.86%		1637	81.56%	81.56%	
	Pending [1]	31	46.27%			80	52.29%			901	55.04%		
SV1	Entering Stage	39	100.00%			79	100.00%			833	100.00%		
	Exclusions	7	17.95%			18	22.78%			157	18.85%		
	Yield of Stage	32	82.05%	56.67%	82.05%	61	77.22%	56.26%	77.22%	676	81.15%	66.19%	81.15%
	Pending	12	37.50%			19	31.15%			215	31.80%		
SV2	Entering Stage	20	100.00%			42	100.00%			461	100.00%		
	Exclusions	1	5.00%			2	4.76%			23	4.99%		
	Yield of Stage	19	95.00%	53.84%	77.95%	40	95.24%	53.58%	73.54%	438	95.01%	62.89%	77.10%
	Pending	7	36.84%			10	25.00%			132	30.14%		
SV3	Entering Stage	12	100.00%			30	100.00%			306	100.00%		
	Exclusions	0	0.00%			3	10.00%			12	3.92%		
	Yield of Stage	12	100.00%	53.84%	77.95%	27	90.00%	48.22%	66.18%	294	96.08%	60.42%	74.08%
	Pending	1	8.33%			2	7.41%			30	10.20%		
	Randomizations	11	91.67%	49.35%	**71.45%**	25	92.59%	44.65%	**61.28%**	264	89.80%	54.26%	**66.52%**

[1] Pending is defined as women still eligible based on current data who have not proceeded to next stage. Percent pending is percent of yield of stage.

Data as of 08/31/94

Table 2.4
Race and Ethnicity Specific Recruitment Yields by Stage

		Hispanics				Whites				Other Ethnicities			
				Cum Yield from				Cum Yield from				Cum Yield from	
Stage	State	N	%	SV0	SV1	N	%	SV0	SV1	N	%	SV0	SV1
SV0	Entering Stage	557	100.00%			24233	100.00%			249	100.00%		
	Exclusions	65	11.67%			7559	31.19%			73	29.32%		
	Yield of Stage	492	88.33%	88.33%		16674	68.81%	68.81%		176	70.68%	70.68%	
	Pending	127	25.81%			7646	45.86%			88	50.00%		
SV1	Entering Stage	384	100.00%			10629	100.00%			102	100.00%		
	Exclusions	42	10.94%			2088	19.64%			15	14.71%		
	Yield of Stage	342	89.06%	78.67%	89.06%	8541	80.36%	55.29%	80.36%	87	85.29%	60.29%	85.29%
	Pending	88	25.73%			2595	30.38%			30	34.48%		
SV2	Entering Stage	253	100.00%			5937	100.00%			56	100.00%		
	Exclusions	22	8.70%			330	5.56%			3	5.36%		
	Yield of Stage	231	91.30%	71.83%	81.32%	5607	94.44%	52.22%	75.89%	53	94.64%	57.06%	80.72%
	Pending	67	29.00%			1252	22.33%			13	24.53%		
SV3	Entering Stage	165	100.00%			4375	100.00%			41	100.00%		
	Exclusions	3	1.82%			131	2.99%			3	7.32%		
	Yield of Stage	162	98.18%	70.52%	79.84%	4244	97.01%	50.65%	73.62%	38	92.68%	52.88%	74.82%
	Pending	25	15.43%			224	5.28%			4	10.53%		
	Randomizations	137	84.57%	59.64%	**67.52%**	4020	94.72%	47.98%	**69.73%**	34	89.47%	47.32%	**66.94%**

Data as of 08/31/94

Table 2.5
Age Specific Recruitment Yields by Stage

		Ages 50-54				Ages 55-59				Ages 60-69				Ages 70-79			
				Cum Yield from				Cum Yield from				Cum Yield from				Cum Yield from	
Stage	State	N	%	SV0	SV1	N	%	SV0	SV1	N	%	SV0	SV1	N	%	SV0	SV1
SV0	Entering Stage	5556	100.00%			5993	100.00%			10798	100.00%			4983	100.00%		
	Exclusions	1546	27.83%			1568	26.16%			3215	29.77%			1764	35.40%		
	Yield of Stage	4020	72.35%	72.35%		4425	73.84%	73.84%		7583	70.23%	70.23%		3219	64.60%	64.60%	
	Pending [1]	1966	48.91%			2038	46.06%			3427	45.19%			1482	46.04%		
SV1	Entering Stage	2403	100.00%			2847	100.00%			4794	100.00%			2016	100.00%		
	Exclusions	471	19.60%			514	18.05%			887	18.50%			434	21.53%		
	Yield of Stage	1932	80.40%	58.17%	80.40%	2333	81.95%	60.51%	81.95%	3907	81.50%	57.23%	81.50%	1582	78.47%	50.69%	78.47%
	Pending	536	27.74%			642	27.52%			1223	31.30%			566	35.78%		
SV2	Entering Stage	1393	100.00%			1689	100.00%			2678	100.00%			1016	100.00%		
	Exclusions	62	4.45%			88	5.21%			159	5.94%			72	7.09%		
	Yield of Stage	1331	95.55%	55.58%	76.82%	1601	94.79%	57.35%	77.68%	2519	94.06%	53.83%	76.66%	944	92.91%	47.10%	72.91%
	Pending	294	22.09%			321	20.05%			570	22.63%			297	31.46%		
SV3	Entering Stage	1043	100.00%			1283	100.00%			1960	100.00%			649	100.00%		
	Exclusions	32	3.07%			34	2.65%			55	2.81%			31	4.78%		
	Yield of Stage	1011	96.93%	53.88%	74.46%	1249	97.35%	55.83%	75.62%	1905	97.19%	52.32%	74.51%	618	95.22%	44.85%	69.43%
	Pending	68	6.73%			71	5.68%			113	5.93%			35	5.66%		
	Randomized	943	93.27%	50.25%	**69.46%**	1178	94.32%	52.66%	**71.32%**	1792	94.07%	49.22%	**70.09%**	583	94.34%	42.31%	65.50%

[1] Pending is defined as women still eligible based on current data who have not proceeded to next stage. Percent pending is percent of yield of stage.

Table 2.6
Clinical Center Ranking by Screening Visit Count

Clinic SV0 Ranking

Rank	Clinic	Organization Name	SV0 Count
1	IOWACITY	Preventive Intervention Center	3477
2	SEATTLE	WHI Seattle Clinical Center	2762
3	MINNEAPO	Berman Center for Clinical Research	2299
4	BIRMING	UAB Preventive Medicine	2263
5	ATLANTA	Emory University Women's Health Initiati	2221
6	BRIGHAM	Brigham and Women's Hospital	2135
7	UCDAVIS	General Internal Medicine	2115
8	CHICAGO	WHI Clinic Northwestern Univ Med School	1557
9	TUCSON	Arizona Disease Prevention Center	1528
10	MEMPHIS	UT Prevention Center, Memphis	1419
11	BUFFALO	WNY Vanguard Clinical Center	1390
12	PAWTUCK	Women's Health Initiative	1091
13	LAJOLLA	UCSD's Women's Health Initiative VCC	1001
14	BOWMAN	Women's Health Initiative of the Triad	982
15	NEWARK	Newark WHI Center	815
16	PITTSBUR	Pittsburgh WHI Center	777
SV0 Totals			27832

Table 2.7

Clinical Center Ranking by Screening Visit Count

Clinic SV1 Ranking

Current SV1 Goal (62 per month since October 01, 1993): 680

Rank	Clinic	Organization Name	SV1 Count	SV1 Goal	SV1 Percent of Goal
1	PITTSBUR	Pittsburgh WHI Center	1353	680	198.97
2	TUCSON	Arizona Disease Prevention Center	1010	680	148.53
3	MEMPHIS	UT Prevention Center, Memphis	1004	680	147.65
4	CHICAGO	WHI Clinic Northwestern Univ Med School	979	680	143.97
5	NEWARK	Newark WHI Center	965	680	141.91
6	MINNEAPO	Berman Center for Clinical Research	963	680	141.62
7	SEATTLE	WHI Seattle Clinical Center	814	680	119.71
8	UCDAVIS	General Internal Medicine	767	680	112.79
9	BIRMING	UAB Preventive Medicine	741	680	108.97
10	BOWMAN	Women's Health Initiative of the Triad	729	680	107.21
11	IOWACITY	Preventive Intervention Center	728	680	107.06
12	LAJOLLA	UCSD's Women's Health Initiative VCC	726	680	106.76
13	BUFFALO	WNY Vanguard Clinical Center	568	680	83.53
14	BRIGHAM	Brigham and Women's Hospital	560	680	82.35
15	PAWTUCK	Women's Health Initiative	501	680	73.68
16	ATLANTA	Emory University Women's Health Initiati	450	680	66.18
SV1 Totals			12858	10880	118.18

Table 2.8

Clinical Center Ranking by Screening Visit Count

Clinic SV2 Ranking

Current SV2 Goal (50 per month since November 01, 1993): 498

Rank	Clinic	Organization Name	SV2 Count	SV2 Goal	SV2 Percent of Goal
1	PITTSBUR	Pittsburgh WHI Center	515	498	103.41
2	SEATTLE	WHI Seattle Clinical Center	512	498	102.81
3	MINNEAPO	Berman Center for Clinical Research	498	498	100.00
4	IOWACITY	Preventive Intervention Center	489	498	98.19
5	MEMPHIS	UT Prevention Center, Memphis	486	498	97.59
6	TUCSON	Arizona Disease Prevention Center	444	498	89.16
7	LAJOLLA	UCSD's Women's Health Initiative VCC	442	498	88.76
8	BOWMAN	Women's Health Initiative of the Triad	441	498	88.55
9	PAWTUCK	Women's Health Initiative	441	498	88.55
10	BUFFALO	WNY Vanguard Clinical Center	423	498	84.94
11	BIRMING	UAB Preventive Medicine	416	498	83.53
12	UCDAVIS	General Internal Medicine	415	498	83.33
13	NEWARK	Newark WHI Center	389	498	78.11
14	BRIGHAM	Brigham and Women's Hospital	385	498	77.31
15	CHICAGO	WHI Clinic Northwestern Univ Med School	376	498	75.50
16	ATLANTA	Emory University Women's Health Initiati	345	498	69.28
SV2 Totals			7017	7968	88.06

Table 2.9

Clinical Center Ranking by Screening Visit Count

Clinic SV3 Ranking

Current SV3 Goal (47 per month since December 01, 1993): 421

Rank	Clinic	Organization Name	SV3 Count	SV3 Goal	SV3 Percent of Goal
1	MINNEAPO	Berman Center for Clinical Research	400	421	95.01
2	SEATTLE	WHI Seattle Clinical Center	387	421	91.92
3	MEMPHIS	UT Prevention Center, Memphis	380	421	90.26
4	PAWTUCK	Women's Health Initiative	365	421	86.70
5	IOWACITY	Preventive Intervention Center	333	421	79.10
6	LAJOLLA	UCSD's Women's Health Initiative VCC	329	421	78.15
7	BOWMAN	Women's Health Initiative of the Triad	323	421	76.72
8	BRIGHAM	Brigham and Women's Hospital	323	421	76.72
9	PITTSBUR	Pittsburgh WHI Center	320	421	76.01
10	NEWARK	Newark WHI Center	317	421	75.30
11	BUFFALO	WNY Vanguard Clinical Center	307	421	72.92
12	BIRMING	UAB Preventive Medicine	302	421	71.73
13	UCDAVIS	General Internal Medicine	293	421	69.60
14	CHICAGO	WHI Clinic Northwestern Univ Med School	252	421	59.86
15	TUCSON	Arizona Disease Prevention Center	223	421	52.97
16	ATLANTA	Emory University Women's Health Initiati	218	421	51.78
SV3 Totals			5072	6736	75.30

Data As Of: 08/31/94

Table 2.10

Randomization Activity by Study Component and Month

Year	Month	HORMONE REPLACEMENT THERAPY RANDOMIZATIONS Goal per Month = 269.6				DIET MODIFICATION RANDOMIZATIONS Goal per Month = 517.3				TOTAL CLINICAL TRIAL RANDOMIZATIONS					
		Number	Cum. #	Cum. Goal	% of Cum. Goal	Number	Cum. #	Cum. Goal	% of Cum. Goal	CT #	CT Cum. #	HRT/DM #	HRT/DM Cum. #	% Overlap	% Cum. Overlap
1993	September	0	0	0.0	0.00%	0	0	0.0	0.00%	0	0	0	0	0.00%	0.00%
	October	0	0	0.0	0.00%	1	1	0.0	0.00%	1	1	0	0	0.00%	0.00%
	November	3	3	0.0	0.00%	7	8	0.0	0.00%	8	9	2	2	25.00%	22.22%
	December	30	33	269.6	12.24%	45	53	517.3	10.24%	62	71	13	15	20.97%	21.13%
1994	January	65	98	539.2	18.18%	125	178	1034.7	17.20%	166	237	24	39	14.46%	16.46%
	February	77	175	808.7	21.64%	186	364	1552.0	23.45%	235	472	28	67	11.91%	14.19%
	March	137	312	1078.3	28.93%	379	743	2069.3	35.91%	451	923	65	132	14.41%	14.30%
	April	186	498	1347.9	36.95%	458	1201	2586.7	46.43%	560	1483	84	216	15.00%	14.57%
	May	226	724	1617.5	44.76%	598	1799	3104.0	57.96%	737	2220	87	303	11.80%	13.65%
	June	240	964	1887.0	51.09%	668	2467	3621.3	68.12%	806	3026	102	405	12.66%	13.38%
	July	223	1187	2156.6	55.04%	552	3019	4138.7	72.95%	671	3697	104	509	15.50%	13.77%
	August	260	1447	2426.2	59.64%	646	3665	4656.0	78.72%	799	4496	107	616	13.39%	13.70%

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Table 2.11

Clinical Center Randomization Activity with Ranking by Number of Participants Randomized

Data As Of: 08/31/94

Randomizations For Month: AUG 94

		HORONONE REPLACEMENT THERAPY RANDOMIZATIONS (Monthly Goal Per Clinic = 16.8) (Cumulative Monthly Goal = 151.6)			DIET MODIFICATION RANDOMIZATIONS (Monthly Goal Per Clinic = 32.3) (Cumulative Monthly Goal = 291.0)			TOTAL CLINICAL TRIAL RANDOMIZATIONS					
Rank	Clinic	Number	Cum. #	% of Cum. Goal	Number	Cum. #	% of Cum. Goal	CT #	CT Cum. #	HRT/DM #	HRT/DM Cum. #	% Overlap	% Cum. Overlap
1	MINNEAPO	13	104	68.59%	42	311	106.87%	49	372	6	43	12.24%	11.56%
2	SEATTLE	12	79	52.10%	47	311	106.87%	57	359	2	31	3.51%	8.64%
3	MEMPHIS	13	135	89.03%	40	260	89.35%	48	338	5	57	10.42%	16.86%
4	PAWTUCK	15	124	81.77%	21	252	86.60%	31	330	5	46	16.13%	13.94%
5	BRIGHAM	9	62	40.89%	37	275	94.50%	42	312	4	25	9.52%	8.01%
6	IOWACITY	35	162	106.83%	47	208	71.48%	71	305	11	65	15.49%	21.31%
7	BIRMING	30	116	76.50%	55	238	81.79%	69	283	16	71	23.19%	25.09%
8	PITTSBUR	11	120	79.14%	17	204	70.10%	24	280	4	44	16.67%	15.71%
9	UCDAVIS	18	69	45.50%	50	234	80.41%	61	279	7	24	11.48%	8.60%
10	BUFFALO	11	72	47.48%	45	239	82.13%	52	278	4	33	7.69%	11.87%
11	BOWMAN	14	90	59.35%	45	227	78.01%	54	277	5	40	9.26%	14.44%
12	LAJOLLA	19	96	63.31%	34	226	77.66%	43	272	10	50	23.26%	18.38%
13	CHICAGO	9	45	29.68%	38	200	68.73%	43	229	4	16	9.30%	6.99%
14	ATLANTA	28	60	39.57%	42	175	60.14%	56	206	14	29	25.00%	14.08%
15	NEWARK	9	63	41.55%	46	157	53.95%	50	196	5	24	10.00%	12.24%
16	TUCSON	14	50	32.97%	40	148	50.86%	49	180	5	18	10.20%	10.00%
Totals		260	1447	59.64%	646	3665	78.72%	799	4496	107	616	13.39%	13.70%

Table 2.12

Reasons for Refusing/Revoking Consent
By Study Component

Data as of: 08/31/94

Reason Group	Screening Consent Refused/Revoked Count	Screening Consent Percent Refused/Revoked	HRT Consent Refused/Revoked Count	HRT Consent Percent Refused/Revoked	DM Consent Refused/Revoked Count	DM Consent Percent Refused/Revoked
CONFLICTS	88	4.43	190	4.58	20	1.70
CONTACTS	185	9.32	13	0.31	208	17.72
LIMITATIONS	254	12.80	1435	34.62	156	13.29
LOST CONTACT/DIED	5	0.25	2	0.05	0	0.00
OTHER	601	30.28	878	21.18	289	24.62
PERSONAL	256	12.90	74	1.79	190	16.18
PROCEDURES	11	0.55	16	0.39	26	2.21
REASON NOT GIVEN	242	12.19	346	8.35	181	15.42
REFUSAL	230	11.59	140	3.38	68	5.79
TRAVEL	192	9.67	38	0.92	126	10.73
TREATMENTS	81	4.08	369	8.90	4	0.34
WORRIES	76	3.83	771	18.60	5	0.43

Consent Form Summary

Consent Name	Forms	Signed	%	Refused	%	Revoked	%	Unanswered	%
SCREENING CONSENT	13534	11533	85.22	1683	12.44	302	2.23	16	.12
HRT CONSENT	6605	2442	36.97	3961	59.97	184	2.79	18	.27
DMT CONSENT	6609	5423	82.05	869	13.15	305	4.61	12	.18

3. Baseline Characteristics

3.1. Design Parameters and Study Goals

Age and, for HRT, hysterectomy status are important design factors in determining the required sample size for the CT. *Table 3.1. - Randomization/Enrollment Summary by Study Component, Age and Hysterectomy Status* displays the distribution of age and hysterectomy status by study component. Note that the prescribed age distribution for each component is 10%, 15%, 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 is to be limited to 30%.

The study has a clear deficit in the oldest age category; only 13.5% of HRT participants and 12.5% of DM participants are 70-79 years of age. With respect to uterine status, 42% of women randomized to HRT have had hysterectomies. While there is some variability in the degree, the trend is uniform across VCCs. At the August 2, 1994 Executive Committee meeting, VCCs were asked to begin targeting older women through preferential recruitment and screening of these women.

Race and ethnicity goals have been defined to assure the study's ability to address particular questions in minority populations. The study-wide goal is 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 Tuscon (Hispanic and Native American).

Race and ethnicity are determined by self-report on *Form 2/3 - Eligibility Screen* in accordance with the U.S. Census defined categories. *Table 3.2. - Distribution of Race and Ethnicity Among Randomized/Enrolled Participants by Clinical Center* presents the distribution of race and ethnicity among all women randomized or enrolled to WHI by CC and funding category (Pool 1 or 2).

Among Pool 1 VCCs, 21% of currently recruited women are from racial or ethnic minorities, with most of these being either Hispanic (11.7%) or Black/African American (7.8%). Among Pool 2 VCCs, minority women represent 7.6% of the accrued population. To address the low representation of minority women, the Executive Committee in August 1994 formed a Minority Recruitment Task Force and charged it with identifying the barriers to and methods for enhancing minority recruitment.

3.2. Selected Baseline Predictors

To further characterize the recruited population, *Tables 3.3.-3.11. - Questionnaire Responses by Enrollment Status* present the distributions of selected baseline variables (race/ethnicity, marital status, income, education, ever smoker, alcohol, parity, age at first pregnancy, family

history of breast cancer) by study component. The exact wording of associated questions can be found by referring to the WHI form indicated at the bottom of each page.

Table 3.12. - Physical Measures by Enrollment Status presents distributions of weight, height, body mass index and blood pressure in randomized women.

Table 3.1

Randomization/Enrollment Summary
By Study Component, Age and Hysterectomy Status

HRT Randomization Summary

Study Component	Age Range	Randomized in August	Total Randomized	Age Distribution	Cum. Goal Through Aug.	Percent of Goal
HRT/Hysterectomy	50-54	17	99	16.3	74.2	133.46
	55-59	20	127	20.9	144.0	88.19
	60-69	57	286	47.0	327.3	87.39
	70-79	16	96	15.8	183.3	52.38
	Subtotal	110	608	100.0	728.7	83.43
HRT/Non-Hysterectomy	50-54	24	134	16.0	170.2	78.74
	55-59	38	215	25.6	340.4	63.17
	60-69	68	390	46.5	763.6	51.07
	70-79	20	100	11.9	423.3	23.63
	Subtotal	150	839	100.0	1697.5	49.43
	HRT Total	260	1447		2426.2	59.64

DM Randomization Summary

Study Component	Age Range	Randomized in August	Total Randomized	Age Distribution	Cum. Goal Through Aug.	Percent of Goal
DM	50-54	133	819	22.3	466.9	175.41
	55-59	177	992	27.1	929.5	106.73
	60-69	240	1397	38.1	2094.5	66.70
	70-79	96	457	12.5	1165.1	39.22
	DM Total	646	3665	100.0	4656.0	78.72

Observational Study Enrollment Summary

Study Component	Age Range	Enrollment in August	Cummulative Enrollment	Age Distribution
OS	50-54	0	0	0.0
	55-59	0	0	0.0
	60-69	0	0	0.0
	70-79	0	0	0.0
	Total	0	0	0.0

Table 3.2

Distribution of Race and Ethnicity among
Randomized/Enrolled Participants by Clinical Center

Data As Of: 08/31/94

	Am. Indian/ Alaskan Native Rand/Enrollments Actual #	Actual %	Asian/Pacific Islander Rand/Enrollments Actual #	Actual %	Black/African American Rand/Enrollments Actual #	Actual %	Hispanic Rand/Enrollments Actual #	Actual %	White Rand/Enrollments Actual #	Actual %	Other Rand/Enrollments Actual #	Actual %	Total Rand/Enroll Actual #
Pool 1													
ATLANTA	1	0.5	2	1.0	21	10.2	1	0.5	180	87.4	1	0.5	206
BIRMING	1	0.4	0	0.0	44	15.5	0	0.0	238	84.1	0	0.0	283
LAJOLLA	1	0.4	3	1.1	3	1.1	75	27.6	185	68.0	5	1.8	272
TUCSON	1	0.6	1	0.6	5	2.8	34	18.9	138	76.7	1	0.6	180
Sub Total	4	0.4	6	0.6	73	7.8	110	11.7	741	78.7	7	0.7	941
Pool 2													
BOWMAN	1	0.4	0	0.0	31	11.2	2	0.7	242	87.4	1	0.4	277
BRIGHAM	0	0.0	2	0.6	16	5.1	3	1.0	288	92.6	2	0.6	311
BUFFALO	1	0.4	0	0.0	11	4.0	0	0.0	265	95.3	1	0.4	278
CHICAGO	0	0.0	3	1.3	17	7.4	3	1.3	205	89.5	1	0.4	229
IOWACITY	0	0.0	0	0.0	2	0.7	1	0.3	302	99.0	0	0.0	305
MEMPHIS	0	0.0	0	0.0	43	12.8	1	0.3	290	86.6	1	0.3	335
MINNEAPO	1	0.3	1	0.3	5	1.3	2	0.5	362	97.3	1	0.3	372
NEWARK	0	0.0	0	0.0	33	16.8	2	1.0	160	81.6	1	0.5	196
PAWTUCK	0	0.0	0	0.0	3	0.9	1	0.3	320	97.3	5	1.5	329
PITTSBUR	1	0.4	0	0.0	10	3.6	1	0.4	266	95.0	2	0.7	280
SEATTLE	0	0.0	3	0.8	12	3.3	2	0.6	335	93.3	7	1.9	359
UCDAVIS	3	1.1	10	3.6	8	2.9	9	3.2	244	87.5	5	1.8	279
Sub Total	7	0.2	19	0.5	191	5.4	27	0.8	3279	92.4	27	0.8	3550
TOTAL	11	0.2	25	0.6	264	5.9	137	3.1	4020	89.5	34	0.8	4491

Data as of: 08/31/94

Table 3.3

Questionnaire Responses By Enrollment Status

Short Verbiage	Question Response	Response Meaning	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Racial or ethnic group	1	American Indian or Alaskan Native	2	0.2	8	0.3	1	0.2
	2	Asian or Pacific Islander	6	0.7	17	0.6	2	0.3
	3	Black or African-American	47	5.7	175	5.7	42	6.8
	4	Hispanic	34	4.1	77	2.5	26	4.2
	5	White	734	88.3	2744	90.0	542	88.0
	8	Other	6	0.7	25	0.8	3	0.5
		Value not entered	2	0.2	3	0.1	0	0.0
	Total		831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1218	2	1	105	Racial or ethnic group
2532	2	2	18	Racial or ethnic group

Data as of: 08/31/94

Table 3.4

Questionnaire Responses By Enrollment Status

Short Verbiage	Question Response	Response Meaning	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Marital status	1	Never married	29	3.5	134	4.4	20	3.2
	2	Divorced or separated	146	17.6	418	13.7	90	14.6
	3	Widowed	131	15.8	373	12.2	100	16.2
	4	Presently married	509	61.3	2073	68.0	399	64.8
	5	Living in a marriage-like relationship	11	1.3	47	1.5	6	1.0
		Questionnaire not entered	2	0.2	1	0.0	0	0.0
		Value not entered	3	0.4	3	0.1	1	0.2
	Total		831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1745	20	1	25	Marital status

Table 3.5

Questionnaire Responses By Enrollment Status

Short Verbiage	Question Response	Response Meaning	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Total family income	1	Less than $10,000	55	6.6	89	2.9	39	6.3
	2	$10,000 to $19,999	123	14.8	305	10.0	92	14.9
	3	$20,000 to $34,999	221	26.6	687	22.5	182	29.5
	4	$35,000 to $49,999	161	19.4	689	22.6	118	19.2
	5	$50,000 to $74,999	135	16.2	608	19.9	115	18.7
	6	$75,000 to $99,999	51	6.1	272	8.9	32	5.2
	7	$100,000 to $149,999	30	3.6	164	5.4	12	1.9
	8	$150,000 or more	15	1.8	83	2.7	7	1.1
	9	Don't know	19	2.3	68	2.2	9	1.5
		Questionnaire not entered	2	0.2	1	0.0	0	0.0
		Value not entered	19	2.3	83	2.7	10	1.6
	Total		831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1755	20	1	34	Total family income

Table 3.6

Questionnaire Responses By Enrollment Status

Short Verbiage	Question Response	Response Meaning	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Highest grade in school	1	Didn't go to school	1	0.1	0	0.0	0	0.0
	2	Grade school (1-4 years)	14	1.7	5	0.2	6	1.0
	3	Grade school (5-8 years)	16	1.9	24	0.8	13	2.1
	4	Some high school (9-11 years)	42	5.1	69	2.3	33	5.4
	5	High school diploma or G.E.D.	161	19.4	498	16.3	148	24.0
	6	Vocational or training school	96	11.6	273	9.0	75	12.2
	7	Some college or Associate Degree	221	26.6	971	31.8	157	25.5
	8	College graduate or Baccalaureate	84	10.1	352	11.5	55	8.9
	9	Some college after college graduation	86	10.3	362	11.9	55	8.9
	10	Master's Degree	90	10.8	438	14.4	66	10.7
	11	Doctoral Degree	15	1.8	52	1.7	7	1.1
		Questionnaire not entered	2	0.2	1	0.0	0	0.0
		Value not entered	3	0.4	4	0.1	1	0.2
	Total		831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1741	20	1	20	Highest grade in school

Table 3.7

Questionnaire Responses By Enrollment Status

Data as of: 08/31/94

Short Verbiage	Question Response	Response Meaning	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Smoked 100 cigarettes	0	No	421	50.7	1487	48.8	320	51.9
	1	Yes	401	48.3	1533	50.3	291	47.2
		Questionnaire not entered	7	0.8	23	0.8	3	0.5
		Value not entered	2	0.2	6	0.2	2	0.3
	Total		831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
2019	34	1	8	Smoked 100 cigarettes

Data as of: 08/31/94

Table 3.8

Questionnaire Responses By Enrollment Status

Short Verbiage	Question Response	Response Meaning	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
12 alcoholic drinks ever	0	No	97	11.7	298	9.8	104	16.9
	1	Yes	726	87.4	2723	89.3	509	82.6
		Questionnaire not entered	7	0.8	23	0.8	3	0.5
		Value not entered	1	0.1	5	0.2	0	0.0
	Total		831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
2039	34	1	28	12 alcoholic drinks ever

Table 3.9

Questionnaire Responses by Enrollment Status

Short Verbiage	Response Range	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Live births	None	17	2.0	59	1.9	11	1.8
	1	68	8.2	282	9.2	45	7.3
	2	183	22.0	789	25.9	140	22.7
	3	214	25.8	760	24.9	156	25.3
	4	143	17.2	461	15.1	82	13.3
	5	66	7.9	188	6.2	70	11.4
	6	33	4.0	117	3.8	30	4.9
	7	22	2.6	43	1.4	15	2.4
	8 or more	23	2.8	44	1.4	18	2.9
	No value entered	62	7.5	306	10.0	49	8.0
	Total	831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1775	31	1	12	Live births

Table 3.10

Questionnaire Responses by Enrollment Status

Short Verbiage	Response Range	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Age first full-term pregnancy	Less than 20	115	13.8	367	12.0	116	18.8
	20-24	366	44.0	1341	44.0	268	43.5
	25-29	193	23.2	722	23.7	132	21.4
	30-34	62	7.5	189	6.2	29	4.7
	35-39	10	1.2	47	1.5	5	0.8
	40-44	2	0.2	3	0.1	0	0.0
	No value entered	83	10.0	380	12.5	66	10.7
	Total	831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1773	31	1	10	Age first full-term pregnancy

Table 3.11

Questionnaire Responses By Enrollment Status

Short Verbiage	Question Response	Response Meaning	HRT Only	HRT Pct	DM Only	DM Pct	HRT /DM	HRT/DM Pct
Female relatives breast cancer	0	No	265	31.9	827	27.1	168	27.3
	1	Yes	126	15.2	510	16.7	88	14.3
	9	Don't know	6	0.7	51	1.7	12	1.9
		Questionnaire not entered	4	0.5	14	0.5	3	0.5
		Value not entered	430	51.7	1647	54.0	345	56.0
	Total		831	100.0	3049	100.0	616	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1895	32	1	89	Female relatives breast cancer

Data As Of: 08/31/94

Table 3.12

Physical Measures by Enrollment Status

	HORMONE REPLACEMENT THERAPY			DIET MODIFICATION			TOTAL		
Measure	N	Mean	SE	N	Mean	SE	N	Mean	SE
WEIGHT KG	1447	74.92	0.39	3665	74.88	0.24	4496	74.39	0.21
HEIGHT CM	1447	161.77	0.16	3665	162.32	0.10	4496	162.22	0.09
BMI	1447	28.63	0.14	3665	28.47	0.10	4496	28.31	0.09
SYSTOLIC 1	1447	129.09	0.47	3665	128.26	0.30	4496	128.33	0.27
DIASTOLIC 1	1447	76.81	0.24	3665	76.73	0.15	4496	76.70	0.14

4. Follow-up Activities

4.1. Overview

Routine follow-up contacts for the CT are designed to ascertain outcomes, assure safety, and assess adherence to interventions. The follow-up schedule consists of annual clinic visits for all CT women, a semi-annual clinic visit 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 six months post-randomization as the designated contact window.

4.2. Adherence to Contact Schedule

Table 4.1. - Adherence to First Semi-Annual Contact by Clinical Center displays adherence to contact schedule by CC for the first semi-annual contact. Data are shown only for women whose contact window was completed by August 31, 1994, indicating that a contact should have occurred.

Current data indicate that 72% of the semi-annual visits required to date have been conducted, with 59% occurring within the 4-week window. There is considerable variability between Clinical Centers on performance of follow-up contacts (between 6% and 100%). The low number of visits due at many VCCs indicate that follow-up activities have not yet become a routine activity. A delay in finalizing some follow-up instruments and in the entering these data contributes to the low number of reported follow-up contacts. VCCs are in the process of completing these data. No data are yet available for the 6 week HRT telephone contact because of the delay in finalizing and implementing the instrument.

4.3. Participation Status

Women may refuse to participate in continued intervention or follow-up activities. Women who withdraw from further intervention are to be 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 submitted on *Form 7 - Participation Status*. Currently, no data are available from this form.

Data As Of: 08/31/94

Table 4.1
Adherence to First Semi-Annual Contact by Clinical Center

Clinic	Number Due*	Number Conducted		Number Conducted In Window**	
ATLANTA	0				
BIRMING	19	15	(78.95%)	13	(68.42%)
BOWMAN	16	5	(31.25%)	1	(6.25%)
BRIGHAM	24	7	(29.17%)	7	(29.17%)
BUFFALO	37	27	(72.97%)	22	(59.46%)
CHICAGO	6	3	(50.00%)	1	(16.67%)
IOWACITY	6	6	(100.00%)	6	(100.00%)
LAJOLLA	24	6	(25.00%)	5	(20.83%)
MEMPHIS	46	37	(80.43%)	36	(78.26%)
MINNEAPO	69	66	(95.65%)	57	(82.61%)
NEWARK	4	3	(75.00%)	2	(50.00%)
PAWTUCK	15	15	(100.00%)	9	(60.00%)
PITTSBUR	27	21	(77.78%)	18	(66.67%)
SEATTLE	3	3	(100.00%)	1	(33.33%)
TUCSON	17	1	(5.88%)	1	(5.88%)
UCDAVIS	38	37	(97.37%)	27	(71.05%)
Totals	351	252	(71.79%)	206	(58.69%)

* Number Due = Members randomized 6.5 months or more ago (calculated from 'Data As Of' date)
** Number Conducted in Window = Members having a first semi-annual visit between 5.5 and 6.5 months after randomization

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 the routine follow-up clinic visits using the number of tablets remaining in the returned bottles and the length of interval between visits. Changes to study medications can occur because of hormone-related symptoms, other adverse effects, or hysterectomy. These changes can be to change dose, to add progesterone, change to an open-label hormone, or change to another blinded study hormone (from PERT to ERT after a hysterectomy).

Because of the limited number of follow-up visits conducted to date, we report only on the study-wide results. Of 152 women with HRT medication adherence data available at the first semi-annual follow-up visit, the average proportion of tablet consumption at six months was 94.6%. Four women have had some change in their study hormone prescription.

5.2. Symptoms

Women may report symptoms potentially related to HRT at any routine follow-up contact or through a non-routine contact with the CC. The primary symptoms being monitored are bleeding and breast changes.

Of the 102 HRT participants with uteri and data reported from their first semi-annual visit, 8.8% report bleeding. One HRT participant has reported breast changes and one has reported other symptoms at the first semi-annual visit. There have been 35 reports of bleeding, one report of breast changes and one report of other symptoms from non-routine contacts of HRT participants.

5.3. Adverse Effects

There has been one adverse effect (deep vein thrombosis) reported.

5.4. Unblinding

Unblinding to HRT is indicated for management of severe symptoms and for serious adverse effects. As of August 31, 1994, 11 HRT participants' assignments had been unblinded, 10 as a response to reported symptoms and one related to procedural errors.

6. Dietary 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 in assigning those women randomized in the Dietary Change (intervention) arm into an intervention group. Ideally, all women in the Dietary Change arm should start intervention sessions within 12 weeks of randomization. Women waiting 20 weeks or more must be classified as minimal participants and other remedial action must be taken. See *WHI Manuals, Vol 2 - Procedures, Section 6.10.6. - Levels of DM Intervention Participation* for further details.

Tables 6.1. - Waiting Time for Start of Intervention Among DM Intervention Participants and *6.2. - DM Participants Awaiting Intervention Start-Up* display the timeliness of initiating intervention by Clinical Center. *Table 6.1.* shows the length of time women waited between being randomized and starting intervention. Of the 1,455 women randomized to DM intervention, 781 have started intervention. Of the 781 women who have started intervention, 678 (86.8%) started within 12 weeks post-randomization. *Table 6.2.* shows the number of women waiting to start intervention. Of 1,455 DM participants randomized to the Dietary Change arm, 674 (46.3%) are awaiting group assignment and the start of intervention. Of the women awaiting intervention startup, 130 (19.3%) have been waiting 12 weeks or more and 62 (9.2%) have been waiting 16 weeks or more.

6.2. Adherence to the Intervention Program

Adherence to the DM intervention is assessed by attendance to group intervention sessions, and by self-monitoring reports of fat, fruit, vegetable, and grain scores. *Table 6.3. - Dietary Modification Session Adherence Summary* displays the study-wide reports of session attendance and completion (where completion equals group attendance plus make-up attendance), and the average of the self-monitoring scores by session.

Table 6.4. - Percent of Participants Completing Dietary Sessions displays session attendance for each Vanguard Clinical Center.

Attendance study-wide ranges from 97.8% at session 1 to 93.2% at session 7 to 90.4% at session 10 (*Table 6.3.*). Sessions move from weekly to biweekly at session 7 and from biweekly to monthly at session 10. Experience from the Women's Health Trial suggest that attendance will decline when the time interval between sessions becomes longer. Note that scores have not been recorded yet for session 10 pending a change in data recording procedures. This accounts for the low member count for scores at session 10.

The study-wide average fat gram score declined from 47.4 at session 2, when participants begin turning in their fat scores, to 26.8 at session 8 when participants are expected to have met their fat gram goals. Assigned fat gram goals range from 29-37, with 32-34 being most frequently assigned. Fat gram goals are individually defined in Protocol *Section 4.2.2.* from participant height and baseline total energy intake. The CCC monitors fat scores at sessions 8, 12, and 16, with the expectation that participants should have attained their fat gram goals

by session 8. Fat scores are collected and recorded at each session beginning with session 3 so that participants and nutritionists can track progress toward the goal.

The study-wide average fruit/vegetable score was 5.6 servings at session 8 when participants begin turning in their fruit/vegetable scores. This score is already above the DM intervention goal of 5 fruit/vegetable servings daily. Data (member count for scores) are insufficient to evaluate beyond session 9. The CCC monitors fruit/vegetable scores at sessions 12 and 16, with the expectation that participants should have attained their fruit/vegetable goals by session 12. Participants turn in fruit/vegetable scores beginning with session 8 so that they and their nutritionists can track progress toward their goals.

The study-wide average grain score was 4.7 at session 8 when participants begin turning in their grain scores. This score is below the DM intervention goal of six servings daily. Data (member count for scores) are insufficient to evaluate beyond session 9. The CCC monitors grain scores at session 16, with the expectation that participants should have attained their grain goals by session 16. Participants turn in their grain scores beginning with session 8 so that they and their nutritionists can track progress toward their goals.

6.3. Number of Active Groups and Group Sizes

The number of active groups and group sizes are displayed in *Table 6.5. - Number of DM Intervention Women Assigned to Diet Groups at Session 01*. Seventy groups are active, i.e., participants have been assigned to a group. All VCCs have conducted at least one group through session 6. One VCC has conducted at least one group through session 13. No VCCs have conducted session 14 or beyond.

The recommended group size is 8-15 participants, with the ideal range being 10-12 participants. Groups that are too small may lead to staff overload. Groups that are too large lead potentially to poor group dynamics. Forty-four percent of the groups are in the ideal size range. One VCC has two groups that are smaller than the recommended size. One VCC has one group that is larger than the recommended size.

6.4. Comparison of Dietary Intake

Dietary intake in DM is assessed at baseline and post-randomization in both the Intervention and Comparison arms with three instruments: the *FFQ*, the *4DFR*, and the 24 Hour Recall (*24HR*). Currently only baseline values of the *FFQ* are available.

Table 6.1

Women's Health Initiative
Waiting Time for Start of Intervention Among DM Intervention Participants
By Clinical Center

Data as of: 08/31/94

Clinic Name	Randomized to DM/INT	Intervention Started	Pct Total	time from randomization to intervention startup: < 4 Weeks	Pct Total	4-<8 Weeks	Pct Total	8-<12 Weeks	Pct Total	12-<16 Weeks	Pct Total	16+ Weeks	Pct Total
ATLANTA	68	24	35.3	6	25.0	6	25.0	9	37.5	2	8.3	1	4.2
BIRMING	97	31	32.0	6	19.4	12	38.7	6	19.4	3	9.7	4	12.9
BOWMAN	90	41	45.6	11	26.8	14	34.1	12	29.3	3	7.3	1	2.4
BRIGHAM	109	49	45.0	28	57.1	13	26.5	4	8.2	3	6.1	1	2.0
BUFFALO	95	55	57.9	18	32.7	26	47.3	6	10.9	2	3.6	3	5.5
CHICAGO	77	41	53.2	12	29.3	15	36.6	8	19.5	3	7.3	3	7.3
IOWACITY	83	21	25.3	4	19.0	5	23.8	5	23.8	6	28.6	1	4.8
LAJOLLA	89	55	61.8	9	16.4	16	29.1	12	21.8	7	12.7	11	20.0
MEMPHIS	103	69	67.0	30	43.5	26	37.7	8	11.6	3	4.3	2	2.9
MINNEAPO	125	76	60.8	23	30.3	29	38.2	13	17.1	9	11.8	1	1.3
NEWARK	64	37	57.8	13	35.1	11	29.7	9	24.3	2	5.4	1	2.7
PAWTUCK	99	75	75.8	14	18.7	24	32.0	24	32.0	10	13.3	3	4.0
PITTSBUR	81	62	76.5	30	48.4	20	32.3	9	14.5	2	3.2	0	0.0
SEATTLE	122	69	56.6	22	31.9	30	43.5	12	17.4	4	5.8	1	1.4
TUCSON	60	9	15.0	3	33.3	3	33.3	2	22.2	0	0.0	1	11.1
UCDAVIS	93	67	72.0	24	35.8	28	41.8	8	11.9	5	7.5	2	3.0
Totals	1455	781	53.7	253	32.4	278	35.6	147	18.8	64	8.2	36	4.6

Table 6.2

Women's Health Initiative
DM Participants Awaiting Intervention Startup
By Clinical Center

Data As Of: 08/31/94

Clinic Name	Randomized to DM/INT	Awaiting DM Intervention	Pct Total	time since randomization: < 4 Weeks	Pct Total	4-<8 Weeks	Pct Total	8-<12 Weeks	Pct Total	12-<16 Weeks	Pct Total	16+ Weeks	Pct Total
ATLANTA	68	44	64.7	2	4.5	14	31.8	8	18.2	8	18.2	12	27.3
BIRMING	97	66	68.0	2	3.0	22	33.3	19	28.8	13	19.7	10	15.2
BOWMAN	90	49	54.4	2	4.1	16	32.7	16	32.7	13	26.5	2	4.1
BRIGHAM	109	60	55.0	1	1.7	13	21.7	14	23.3	16	26.7	16	26.7
BUFFALO	95	40	42.1	3	7.5	13	32.5	12	30.0	8	20.0	4	10.0
CHICAGO	77	36	46.8	1	2.8	9	25.0	9	25.0	7	19.4	10	27.8
IOWACITY	83	62	74.7	7	11.3	13	21.0	12	19.4	13	21.0	17	27.4
LAJOLLA	89	34	38.2	1	2.9	10	29.4	10	29.4	6	17.6	7	20.6
MEMPHIS	103	34	33.0	1	2.9	15	44.1	11	32.4	5	14.7	2	5.9
MINNEAPO	125	49	39.2	0	0.0	16	32.7	18	36.7	9	18.4	6	12.2
NEWARK	64	27	42.2	0	0.0	16	59.3	5	18.5	3	11.1	3	11.1
PAWTUCK	99	24	24.2	0	0.0	8	33.3	8	33.3	6	25.0	2	8.3
PITTSBUR	81	19	23.5	2	10.5	4	21.1	9	47.4	3	15.8	1	5.3
SEATTLE	122	53	43.4	2	3.8	11	20.8	5	9.4	16	30.2	19	35.8
TUCSON	60	51	85.0	2	3.9	14	27.5	12	23.5	11	21.6	12	23.5
UCDAVIS	93	26	28.0	2	7.7	18	69.2	5	19.2	1	3.8	0	0.0
Totals	1455	674	46.3	28	4.2	212	31.5	173	25.7	138	20.5	123	18.2

Data As Of: 08/31/94

Table 6.3

Dietary Modification Session Adherence Summary

Session ID	Members Assigned	Members Evaluated	Attended Session	Completed Session	Percent Complete	---Fat Scores--- Member Count	Average Grams	---F/V Scores--- Member Count	Average Servings	--Grain Scores-- Member Count	Average Servings
01	810	781	697	764	97.82	1	0.0	0		0	
02	759	708	626	689	97.32	43	47.4	0		0	
03	710	649	568	630	97.07	534	33.7	0		0	
04	667	640	549	620	96.88	595	30.4	0		0	
05	618	579	500	562	97.06	514	28.6	0		0	
06	579	517	433	491	94.97	451	27.3	0		0	
07	539	425	351	396	93.18	370	26.6	8	5.4	8	3.9
08	494	357	282	331	92.72	310	26.8	300	5.6	300	4.7
09	324	266	213	251	94.36	231	26.3	225	5.6	225	4.5
10	232	115	91	104	90.43	4	26.4	4	5.0	4	4.2
11	133	69	52	62	89.86	56	24.1	56	6.7	56	4.9
12	59	21	17	19	90.48	17	24.7	17	5.2	17	5.3
13	10	10	8	8	80.00	7	27.4	7	5.9	7	5.5
14	0	0	0	0	0.00	0		0		0	
15	0	0	0	0	0.00	0		0		0	
16	0	0	0	0	0.00	0		0		0	
17	0	0	0	0	0.00	0		0		0	
18	0	0	0	0	0.00	0		0		0	
19 (Individual)	324	182	0	182	100.00	169	26.8	169	5.8	169	4.6

Table 6.4

Percent of Participants Completing Dietary Sessions
By Clinical Center

Clinic Name	DIETARY INSTRUCTIONAL SESSIONS 01	02	03	04	05	06	07	08	09	10	11	12	13
ATLANTA	100.00	100.00	100.00	100.00	100.00	83.33							
BIRMING	90.32	87.10	88.89	90.32	100.00	88.89	91.67						
BOWMAN	95.12	95.00	100.00	96.67	93.33	95.24	100.00	95.00	100.00	88.89	77.78		
BRIGHAM	100.00	100.00	100.00	97.96	100.00	100.00	97.96	100.00	87.76				
BUFFALO	100.00	100.00	96.36	98.18	96.36	94.55	92.73	85.37	92.31	88.46	81.82	81.82	
CHICAGO	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	87.50	87.50			
IOWACITY	100.00	100.00	100.00	100.00	100.00	100.00	77.78						
LAJOLLA	94.55	98.11	96.15	94.23	96.55	93.10	82.76	75.00					
MEMPHIS	100.00	98.51	95.65	100.00	100.00	97.01	100.00	100.00	100.00	100.00	95.00		
MINNEAPO	100.00	98.68	100.00	100.00	98.48	96.23	94.34	92.11	96.55	77.78	94.74	100.00	80.00
NEWARK	100.00	100.00	100.00	100.00	95.45	100.00	87.50	100.00					
PAWTUCK	94.67	95.24	98.00	94.34	92.86	100.00	96.55	89.66	96.55				
PITTSBUR	100.00	95.08	92.98	98.18	96.36	98.15	96.55	93.10	93.10	93.33			
SEATTLE	92.75	97.62	95.24	92.86	92.86	90.00	82.35	88.89	85.71				
TUCSON	100.00	100.00	88.89	88.89	88.89	77.78	77.78	66.67					
UCDAVIS	100.00	97.01	97.01	96.36	97.67	93.02	88.37	100.00	100.00	94.74	90.00		

Table 6.5

Number of DM Intervention Women Assigned to Diet Groups at Session 01
By Clinical Center

Clinic Name	Number of Groups	Number of Women Assigned in Each Group At Session 01									
		<8 Women	Pct Total	8-9 Women	Pct Total	10-12 Women	Pct Total	13-15 Women	Pct Total	>15 Women	Pct Total
ATLANTA	2	0	0.0	0	0.0	2	100.0	0	0.0	0	0.0
BIRMING	2	0	0.0	0	0.0	0	0.0	1	50.0	1	50.0
BOWMAN	6	0	0.0	0	0.0	6	100.0	0	0.0	0	0.0
BRIGHAM	4	0	0.0	0	0.0	2	50.0	2	50.0	0	0.0
BUFFALO	4	0	0.0	0	0.0	1	25.0	3	75.0	0	0.0
CHICAGO	4	0	0.0	2	50.0	1	25.0	1	25.0	0	0.0
IOWACITY	2	0	0.0	1	50.0	1	50.0	0	0.0	0	0.0
LAJOLLA	4	0	0.0	0	0.0	1	25.0	3	75.0	0	0.0
MEMPHIS	6	0	0.0	1	16.7	4	66.7	1	16.7	0	0.0
MINNEAPO	7	0	0.0	2	28.6	3	42.9	2	28.6	0	0.0
NEWARK	3	0	0.0	1	33.3	0	0.0	2	66.7	0	0.0
PAWTUCK	7	0	0.0	3	42.9	2	28.6	2	28.6	0	0.0
PITTSBUR	6	2	33.3	0	0.0	2	33.3	2	33.3	0	0.0
SEATTLE	6	0	0.0	0	0.0	1	16.7	5	83.3	0	0.0
TUCSON	1	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0
UCDAVIS	6	0	0.0	1	16.7	5	83.3	0	0.0	0	0.0
Totals	70	2	2.9	12	17.1	31	44.3	24	34.3	1	1.4

7. Outcomes

7.1. Overview

Outcomes are ascertained at routine follow-up visits. Initial reports of clinical outcomes are obtained on *Form 33 - Medical History Update* or through routine procedures during the annual visit (e.g., mammography, endometrial aspirations, ECGs). Depending on the type, outcomes may be accepted based on self-report, or local and central adjudication may be required. See *Vol. 2 - Procedures, Section 17 - Outcome Procedures* for further details.

7.2. Initial Report of Outcomes

As of August 31, 1994, *Form 33 - Medical History Update* data were available for 312 women. There were 32 women reporting hospitalizations since randomization. Self-reported outcomes from this form include: heart or circulatory problems--2; cancer--1; stroke/TIA--1.

7.3. Confirmed Outcomes

No outcomes have been confirmed. Documentation and adjudication awaits implementation of outcomes procedures currently under development.

8. Quality Assurance

Data quality in WHI is promoted through standardized documentation and data collection instruments, central training and certification for lead personnel, local training and certification for other staff, checklists, direct observation, database monitoring (edit checks), duplication, and site visits.

To address additional VCC operational concerns beyond those of recruitment and screening, the Executive Committee in December 1993 formed a Streamlining Task Force (STF). One of the charges to the STF was to review the quality assurance program and make recommendations for streamlining. Recommendations for QA from the STF included: focus on high priority items; allow greater flexibility in the local QA implementation; rely more heavily on automated data checks. To meet these objectives, the decisions were made to accept all self-administered forms other than eligibility or outcomes related items without review with the participant and to convert most data collection forms to mark-sense (bubble) format.

8.1. Timeliness of Data

Table 8.1. - Timeliness of Data by Clinical Center summarizes the timeliness of data entry by CC. Acceptable performance is defined as 80% of data entered within 14 days of participant encounter and 95% entered within 30 days. Excellent performance is defined as 90% in 14 days and 98% entered within 30 days. Study-wide performance shows that 72% of data collected are entered within seven days, 84% within 14 days, and 94% within 30 days. Three VCCs (Buffalo, Minneapolis, and Seattle) have achieved excellent performance. Three other VCCs have acceptable performance (Atlanta, Iowa, and Tucson). *Table 8.2. - Timeliness of Data Entry by Form* summarizes timeliness of data entry by form. Forms capturing clinical or lab results are especially prone to data entry delays. This reflects the significant burden many CCs face in obtaining results from outside providers.

8.2. Completeness of Baseline Data

Table 8.3. - Completeness of Data on Randomized Participants summarizes the completeness of baseline data at form level for randomized participants by study component and task (form). Overall, the proportion of women missing a required baseline data form is less than 1%. Note that a WHILMA algorithm checks for entry of all eligibility data and the encounter information (header) for all other baseline forms as a prerequisite to randomization, thus assuring a high level of complete data.

Summaries of missing data at the level of the individual fields have not been prepared. Examples of the frequency of missing values for selected variables may be found in *Tables 3.3.-3.6. -- Questionnaire Responses by Enrollment Status*. For race/ethnicity, marital status, family income and education, the frequencies of missing values ("Value not entered") were 0.1%, 0.2%, 2.5%, and 0.2%, respectively.

8.3. Post-Randomization Changes in Eligibility Data

As noted above, the entry and automated evaluation of all eligibility data is required in WHILMA prior to randomization. CCs have the ability to edit all locally entered data, although warning messages are displayed whenever eligibility data are modified.

Table 8.4. - Post-Randomization Changes in Eligibility Data displays all changes made to eligibility data post-randomization. No participant became ineligible based on these changes. The age stratum for one participant's randomizations to HRT and DM is made incorrect by one change.

8.4. Specimen Data Quality

WHI specimens are defined generically as products collected from participants that require further central processing before data are generated for the study database. Examples of specimens are blood and urine aliquots, electrocardiograms, bone densitometry, *4DFRs*, and endometrial aspirations. These specimens are collected and logged by CC staff and sent directly to the appropriate central processing site. Data are provided to the CCC from the central processing site and the CCC is responsible for linking these data to existing information in WHILMA.

Three CCC subcontractors (Ogden, Epicore, and UCSF) have provided data tracking information as of August 31, 1994. Data presented here show matching rates between WHILMA tracking data and those data provided by the central processing sites. These reports are used to alert the CCC to problems in identifying and retrieving centrally-processed data. The proper identification of all of these products is critical to long term case-control analyses.

Because of the separate processes involved in satellite site operation, tracking reports in this section show site-specific data.

8.4.1. Blood and Urine Specimens

Table 8.5. - Matching Rates for Blood Draw IDs (Received at Ogden) summarizes blood and urine specimens received by Ogden by Clinical Center and the matching rate to *Form 100 - Blood Collection and Processing* entered into WHILMA. As of August 31, Ogden has received specimens from 9,475 blood draws of which 294 could not be matched to WHILMA data. This 3.1% unmatched may be attributable to normal lag time to data entry although labeling problems cannot be ruled out entirely at this time. *Table 8.6. - Matching Rates for Blood Draw IDs (Logged Into WHILMA)* summarizes *Form 100* data in WHILMA and the proportion of these specimens actually received at Ogden. Of 10,073 specimen draws reported in WHLMA, 8.9% have not been received by Ogden. Those specimens not matched probably reflect delays in shipment to Ogden and some confusion about procedures for specimens of women found to be CT ineligible. While this proportion of unmatched specimens is higher than hoped, clarification with some VCCs about their internal procedures should reduce this to an acceptable level.

Each blood draw is designed to produce 12 required aliquots. *Table 8.7. - Percent Complete Blood Sample Aliquots in Storage* summarizes the completeness of blood collection and storage by Clinical Center, based on unique blood draws actually received at the repository. Of these, 96.9% of draws have the complete set of aliquots. The range among Clinical Centers is from 87.7% to 99.7% of specimens. In the case of difficult blood draws, current procedures allow for the collection of only the bloods required for safety analyses (CBCs and triglycerides). Among the 4,496 women randomized, 34 (0.8%) had only safety bloods collected.

Table 8.8. - Matching Rates for Urine Draw IDs (Received at Ogden) summarizes urine specimens received by Ogden from the VCCs participating in the Osteoporosis substudy. Ogden has received specimens from 2,114 collections, of which 2,025 could be identified in WHILMA. The remaining 4.2% that cannot currently be identified is within the range expected from key entry delays. Among those specimens logged into WHILMA, *Table 8.9. - Matching Rates for Urine Collection IDs (Logged Into WHILMA)* indicates that 15.2% have not been received at Ogden. Further tracking of these unmatched specimens is underway. 99% of stored urine specimens have the required number of aliquots.

8.4.2. Electrocardiograms

Table 8.10. - Matching Rates for ECG IDs (Received at Epicore) summarizes the ECGs submitted by CCs to Epicore and the proportion of these matched to *Form 86 - ECG* data in WHILMA. Of the 5,804 ECGs received by Epicore for WHI, 4.8% of the ECGs could not be matched. This value is within the limits expected from normal key-entry delays, but the variation between CCs indicates that attention to local procedures is required. *Table 8.11. - Matching Rates for ECG IDs (Logged Into WHILMA)* summarizes *Form 86* data in WHILMA and the proportion of these ECGs received by Epicore. Of the 6,318 ECGs reported in WHILMA, 12.5% have not been received by Epicore. This value is higher than expected given that ECGs are transmitted electronically from the CCs to Epicore after each group of 10-12 ECGs is obtained. Failure to match is most likely due to using an incorrect study ID number. Additional attention to these procedures is needed to increase the matching rate to an acceptable level.

Quality scores for ECGs are defined on a scale of 1 (highest quality) to 5 (lowest). Epicore assigns a quality score to ECG as part of their central reading. *Table 8.12. - ECG Quality Grades* summarizes quality of ECGs by Clinical Center. Grades 4 and 5 are considered unacceptable grades. Continued follow-up of machinery and technicians is required to reduce the rates of unacceptable ECGs.

8.4.3. Bone Densitometry

Tables 8.13. - Matching Rates for Bone Scan IDs (Received at UCSF) and *8.14. - Matching Rates for Bone Scan IDs (Logged into WHILMA)* provide a summary of bone densitometry tracking data for the three osteoporosis substudy CCs. UCSF has received 1,366 bone scans of which 7.8% could not be matched *to Form 87 - Bone Densitometry* data in WHILMA, again somewhat higher than expected by data entry delays. Of the 1,303 bone scans reported in WHILMA, 3.3% have not been received by UCSF. Since bone scans are submitted only

monthly, this unmatched quantity is well within the limits expected from normal processing delays.

Table 8.1

Timeliness of Data Entry
Study-Wide by Clinical Center

Org ID	Clinic Name	Total Forms	No Data	% of Total	Time From Encounter Date to Key Entry: 0-7 Days	% of Total	8-14 Days	% of Total	15-30 Days	% of Total	30+ Days	% of Total
19	ATLANTA	12274	63	0.5	8782	71.5	2008	16.4	832	6.8	589	4.8
12	BIRMING	14830	12	0.1	7492	50.5	3503	23.6	2700	18.2	1123	7.6
13	BOWMAN	10145	29	0.3	7526	74.2	1045	10.3	925	9.1	620	6.1
14	BRIGHAM	10694	9	0.1	7079	66.2	1263	11.8	1685	15.8	658	6.2
15	BUFFALO	10893	15	0.1	9655	88.6	582	5.3	439	4.0	202	1.9
16	CHICAGO	10835	3	0.0	6660	61.5	1526	14.1	1612	14.9	1034	9.5
21	IOWACITY	14228	5	0.0	11343	79.7	1756	12.3	758	5.3	366	2.6
22	LAJOLLA	9674	94	1.0	7255	75.0	999	10.3	700	7.2	626	6.5
24	MEMPHIS	11601	106	0.9	5285	45.6	3060	26.4	1867	16.1	1283	11.1
25	MINNEAPO	13715	46	0.3	11770	85.8	1247	9.1	497	3.6	155	1.1
26	NEWARK	9950	39	0.4	8234	82.8	437	4.4	632	6.4	608	6.1
23	PAWTUCK	10081	17	0.2	6033	59.8	1004	10.0	1246	12.4	1781	17.7
28	PITTSBUR	13592	88	0.6	9844	72.4	1550	11.4	1191	8.8	919	6.8
18	SEATTLE	12879	25	0.2	11519	89.4	799	6.2	302	2.3	234	1.8
29	TUCSON	10777	54	0.5	8001	74.2	1529	14.2	757	7.0	436	4.0
30	UCDAVIS	15006	87	0.6	11142	74.3	1474	9.8	1393	9.3	910	6.1
Sum		191174	692	0.4	137620	72.0	23782	12.4	17536	9.2	11544	6.0

Table 8.2

Timeliness of Data Entry By Form

Task ID	Task Name	Total Forms	No Data	% of Total	Time From Encounter Date to Key Entry: 0-7 Days	% of Total	8-14 Days	% of Total	15-30 Days	% of Total	30+ Days	% of Total
2	ELIGIBILITY SCREENING	29586	12	0.0	17431	58.9	5374	18.2	3843	13.0	2926	9.9
4	HRT WASHOUT	408	1	0.2	234	57.4	35	8.6	33	8.1	105	25.7
5	ELIGIBILITY REVIEW	10492	3	0.0	8560	81.6	1013	9.7	572	5.5	344	3.3
6	FINAL ELIGIBILITY ASSESS	9053	32	0.4	6881	76.0	725	8.0	753	8.3	662	7.3
11	SCREENING CONSENT	13973	54	0.4	9524	68.2	1936	13.9	1298	9.3	1161	8.3
12	HRT CONSENT	6896	12	0.2	4711	68.3	949	13.8	689	10.0	535	7.8
13	DMT CONSENT	6927	18	0.3	4843	69.9	784	11.3	803	11.6	479	6.9
14	OS CONSENT	53	0	0.0	42	79.2	4	7.5	3	5.7	4	7.5
15	CAD CONSENT	2	1	50.0	1	50.0	0	0.0	0	0.0	0	0.0
20	PERSONAL INFORMATION	11393	14	0.1	9003	79.0	1180	10.4	671	5.9	525	4.6
30	MEDICAL HISTORY	7496	17	0.2	5895	78.6	860	11.5	523	7.0	201	2.7
31	REPRODUCTIVE HISTORY	7475	14	0.2	5897	78.9	834	11.2	527	7.1	203	2.7
32	FAMILY HISTORY	6519	67	1.0	5301	81.3	563	8.6	444	6.8	144	2.2
33	MEDICAL HISTORY UPDATE	312	1	0.3	198	63.5	39	12.5	40	12.8	34	10.9
34	PERSONAL HABITS	6526	80	1.2	5294	81.1	568	8.7	448	6.9	136	2.1
36	DAILY LIFE (1)	851	4	0.5	598	70.3	108	12.7	103	12.1	38	4.5
37	THOUGHTS AND FEELINGS	7443	14	0.2	5892	79.2	769	10.3	527	7.1	241	3.2
38	DAILY LIFE (2)	6108	15	0.2	4843	79.3	600	9.8	451	7.4	199	3.3
50	ON-STUDY BLEEDING	97	1	1.0	64	66.0	4	4.1	6	6.2	22	22.7
60	FOOD FREQUENCY	20720	10	0.0	17018	82.1	2184	10.5	1086	5.2	422	2.0
62	FOUR DAY FOOD RECORD	3839	10	0.3	3358	87.5	240	6.3	146	3.8	85	2.2
80	PHYSICAL MEASUREMENTS	10647	11	0.1	8520	80.0	1098	10.3	649	6.1	369	3.5
81	PELVIC/PAP SMEAR	2206	14	0.6	876	39.7	388	17.6	520	23.6	408	18.5
82	ENDOMETRIAL ASPIRATION	1279	14	1.1	532	41.6	246	19.2	248	19.4	239	18.7
83	ULTRASOUND	200	3	1.5	66	33.0	19	9.5	48	24.0	64	32.0
84	BREAST EXAM	6375	17	0.3	4556	71.5	624	9.8	757	11.9	421	6.6
85	MAMMOGRAM	6604	188	2.8	2983	45.2	935	14.2	1293	19.6	1205	18.2
86	ECG	6348	40	0.6	3738	58.9	1404	22.1	880	13.9	286	4.5
87	BONE DENSITOMETRY	1316	9	0.7	758	57.6	296	22.5	170	12.9	83	6.3
88	OOPHORECTOMY	30	16	53.3	3	10.0	3	10.0	5	16.7	3	10.0
Sum		191174	692	0.4	137620	72.0	23782	12.4	17536	9.2	11544	6.0

Table 8.3

Completeness of Data on Randomized Participants
by Study Component and Required Forms

Data As Of: 08/31/94

Randomizations DM	HRT	CT	Task	Task Name	DM Keyed	%	HRT Keyed	%
3665	1447	4496	2	ELIGIBILITY SCREENING	3665	100.00%	1447	100.00%
			5	ELIGIBILITY REVIEW	3665	100.00%	1447	100.00%
			6	FINAL ELIGIBILITY ASSESSMENT	3665	100.00%	1447	100.00%
			11	SCREENING CONSENT	3665	100.00%	1447	100.00%
			12	HRT CONSENT			1447	100.00%
			13	DMT CONSENT	3665	100.00%		
			20	PERSONAL INFORMATION	3665	100.00%	1447	100.00%
			30	MEDICAL HISTORY	3661	99.89%	1446	99.93%
			31	REPRODUCTIVE HISTORY	3660	99.86%	1445	99.86%
			32	FAMILY HISTORY	3649	99.56%	1439	99.45%
			34	PERSONAL HABITS	3641	99.35%	1437	99.31%
			37	THOUGHTS AND FEELINGS	3657	99.78%	1446	99.93%
			60	FOOD FREQUENCY	3663	99.95%	1446	99.93%
			62	FOUR DAY FOOD RECORD	3665	100.00%		
			80	PHYSICAL MEASUREMENTS	3665	100.00%	1447	100.00%
			81	PELVIC/PAP SMEAR			1447	100.00%
			84	BREAST EXAM	3665	100.00%	1447	100.00%
			85	MAMMOGRAM	3665	100.00%	1447	100.00%
			86	ECG	3647	99.51%	1445	99.86%
			100	BLOOD DRAW	3665	100.00%	1447	100.00%

Table 8.4

Post-Randomization Changes in Eligibility Data

Form ID	Form Version	Field Order	Short Verbiage	Member ID	Original Response	Change Date	Reason For Response Change	Current Value	Criteria Affected	Associated --Study--- HRT	DM
2	2	1	Birth date	13 10823 L	04/24/33	08/02/94	Incorrect date entered previously	04/24/43	AGE >= 50 AND < 80	YES	YES
									MENOPAUSE, DM & OS		YES
									MENOPAUSE, HRT	YES	
6	2	15	DM - BMI > 40	21 10788 H		07/20/94	Diet staff deemed her ineligible due to BMI		BMI		YES
80	1	8	Weight	12 10043 M	60.2	08/10/94	wrong measurement/reweighed	70.2	BMI	YES	YES
81	1	22	Uterine size weeks	14 10076 Y	00	07/20/94	Current information incorrect. Uterine size 6 weeks not 0 weeks.	06	PAP SMEAR / PELVIC EXAM	YES	
81	1	23	Enlarged since last exam	14 10076 Y		07/20/94	Information missing in this field. Correct response is no.	0			
81	1	24	Adnexae	13 10927 X	0	08/26/94	Hard copy of 81 was lost, GYN gave results on phone, hard copy found and is being entered	1	PAP SMEAR / PELVIC EXAM	YES	
81	1	25	Mass	13 10927 X		08/26/94	original hard copy lost and then found	0	PAP SMEAR / PELVIC EXAM	YES	
81	1	28	Date collected	30 10256 N	02/23/93	07/05/94	Year was indicated incorrectly for collection date should be 02/23/94.	02/23/94	PAP SMEAR / PELVIC EXAM	YES	
82	1	1	Date of endometrial aspiration	18 10189 A	02/04/94	08/08/94	NP wrote incorrect date--out of range	02/03/94	ENDOMETRIAL HYPERPLASIA	YES	
85	1	1	Date of mammogram	26 10280 K	02/24/94	07/22/94	error	08/23/93	CANCER, MAMMOGRAM & CBE	YES	YES
85	1	1	Date of mammogram	26 10284 O	10/01/94	07/22/94	error	11/22/93	CANCER, MAMMOGRAM & CBE	YES	YES
85	1	1	Date of mammogram	26 10086 X	09/01/94	07/22/94	error	10/01/93	CANCER, MAMMOGRAM & CBE	YES	YES
85	1	1	Date of mammogram	28 10007 P	10/25/93	06/30/94	NEW MAMMOGRAM	06/14/94	CANCER, MAMMOGRAM & CBE	YES	YES
85	1	1	Date of mammogram	26 10632 R	06/29/94	08/31/94	addendum added following receipt of old films	06/29/94	CANCER, MAMMOGRAM & CBE	YES	YES
85	1	4	Summary of report	19 10913 P	1	07/20/94	update comparison report	0	CANCER, MAMMOGRAM & CBE	YES	YES

Data as of: 08/31/94

Table 8.4 (Cont.)

Post-Randomization Changes in Eligibility Data

Form ID	Form Version	Field Order	Short Verbiage	Member ID	Original Response	Change Date	Reason For Response Change	Current Value	Criteria Affected	Associated --Study--- HRT	DM
85	1	4	Summary of report	14 11416 H	1	08/10/94	Addendum to original mammo report (received &-28-94) indicates no significant interval change in microcalcifications and pt can be followed yearly	0	CANCER, MAMMOGRAM & CBE	YES	YES
85	1	8	Follow-up results	11 10344 N		08/26/94	6 mo followup mammo. results	0	CANCER, MAMMOGRAM & CBE	YES	YES

Table 8.5

Matching Rates for Blood Draw IDs based on Specimens Received at Ogden by Clinical Center

CLINIC	Number of Ogden Draws	Number of Ogden Draws Match/w WHI Forms (ID)	Ogden Draws Not Match/w WHI Forms	% Not Matched
ATLANTA	423	404	19	4.5
BETTENDO	256	251	5	2.0
BIRMING	516	500	16	3.1
BOWMAN	523	491	32	6.1
BRIGHAM	445	443	2	0.4
BUFFALO	520	510	10	1.9
CHICAGO	324	310	14	4.3
EVANSTON	410	373	37	9.0
IOWACITY	379	373	6	1.6
LAJOLLA	567	561	6	1.1
MEMPHIS	662	636	26	3.9
MINNEAPO	638	638	0	0.0
NEWARK	427	426	1	0.2
PAWTUCK	472	445	27	5.7
PITTSBUR	1149	1116	33	2.9
SEATTLE	699	687	12	1.7
TUCSON	467	427	40	8.6
UCDAVIS	598	590	8	1.3
Total	9475	9181	294	3.1

Table 8.6

Matching Rates for Blood Draw Ids based on Specimens
Logged into WHILMA, by Clinical Center

Data As Of: 08/31/94

CLINIC	Number of WHI Specimen Forms	Number of WHI Specimen Forms Match/w Ogden (ID,Date)	WHI Specimen Forms Not Match/w Ogden Number	% Not Matched
ATLANTA	404	404	0	0.0
BETTENDO	274	251	23	8.4
BIRMING	535	500	35	6.5
BOWMAN	584	491	93	15.9
BRIGHAM	463	443	20	4.3
BUFFALO	524	510	14	2.7
CHICAGO	345	310	35	10.1
EVANSTON	375	373	2	0.5
IOWACITY	373	373	0	0.0
LAJOLLA	595	561	34	5.7
MEMPHIS	637	636	1	0.2
MINNEAPO	662	638	24	3.6
NEWARK	609	426	183	30.0
PAWTUCK	457	445	12	2.6
PHOENIX	96	0	96	100.0
PITTSBUR	1129	1116	13	1.2
SEATTLE	701	687	14	2.0
TUCSON	633	428	205	32.4
UCDAVIS	677	589	88	13.0
Totals	10073	9181	892	8.9

Data as of: 08/31/94

Table 8.7

Percent Complete Blood Sample Aliquots in Storage by Clinic Center

CLINIC	Clinic Total	Total Complete	% Complete
MINNEAPO	638	636	99.7
PAWTUCK	472	469	99.4
UCDAVIS	598	592	99.0
MEMPHIS	662	655	98.9
BRIGHAM	445	440	98.9
CHICAGO	324	320	98.8
IOWACITY	379	374	98.7
EVANSTON	410	403	98.3
PITTSBUR	1149	1127	98.1
BUFFALO	520	510	98.1
BIRMING	516	502	97.3
BETTENDO	256	248	96.9
NEWARK	427	412	96.5
LAJOLLA	567	543	95.8
ATLANTA	423	403	95.3
SEATTLE	699	647	92.6
TUCSON	467	428	91.6
BOWMAN	523	472	90.2
Totals	9475	9181	96.9

Data As Of: 08/31/94

Table 8.8

Matching Rates for Urine Draw IDs based on Specimens Received at Ogden by Clinical Center

CLINIC	Number of Ogden Draws	Number of Ogden Draws Match/w WHI Forms (ID)	Ogden Draws Not Match/w WHI Forms	% Not Matched
BIRMING	515	493	22	4.3
PITTSBUR	1143	1137	6	0.5
TUCSON	456	395	61	13.4
Total	2114	2025	89	4.2

Table 8.9

Matching Rates for Urine Collection IDs based on Specimens Logged into WHILMA, by Clinical Center

Data As Of: 08/31/94

CLINIC	Number of WHI Specimen Forms	Number of WHI Specimen Forms Match/w Ogden (ID,Date)	WHI Specimen Forms Not Match/w Ogden Number	% Not Matched
BIRMING	529	493	36	6.8
PHOENIX	83	0	83	100.0
PITTSBUR	1192	1137	55	4.6
TUCSON	582	394	188	32.3
Totals	2386	2024	362	15.2

Table 8.10

Matching Rates for ECG IDs based on ECGs Received at Epicore, by Clinical Center

Date as of: 08/31/94

CLINIC	Number of Epicore ECG's	Number of Epicore ECG's Match/w WHI ECG Forms (ID,Date)	Epicore ECG's Not Match/w WHI ECG Forms	% Not Matched
ATLANTA	304	274	30	9.9
BETTENDO	170	167	3	1.8
BIRMING	360	354	6	1.7
BOWMAN	331	314	17	5.1
BRIGHAM	341	333	8	2.3
BUFFALO	365	314	51	14.0
CHICAGO	135	131	4	3.0
EVANSTON	173	168	5	2.9
IOWACITY	252	249	3	1.2
LAJOLLA	355	342	13	3.7
MEMPHIS	416	398	18	4.3
MINNEAPO	465	464	1	0.2
NEWARK	264	241	23	8.7
PAWTUCK	388	375	13	3.4
PHOENIX	12	9	3	25.0
PITTSBUR	466	457	9	1.9
SEATTLE	402	376	26	6.5
TUCSON	266	241	25	9.4
UCDAVIS	339	320	19	5.6
Totals	5804	5527	277	4.8

Table 8.11

Matching Rates for ECG IDs based on ECGs Logged into WHILMA, by Clinical Center

Data as of: 08/31/94

CLINIC	Number of WHI ECG Forms	Number of WHI ECG Forms Match/w Epicore ECG's (ID,Date)	WHI ECG Forms Not Match/w Epicore ECG's	% Not Matched
ATLANTA	293	274	19	6.5
BETTENDO	197	167	30	15.2
BIRMING	371	354	17	4.6
BOWMAN	397	314	83	20.9
BRIGHAM	353	333	20	5.7
BUFFALO	361	314	47	13.0
CHICAGO	154	131	23	14.9
EVANSTON	188	168	20	10.6
IOWACITY	268	249	19	7.1
LAJOLLA	409	342	67	16.4
MEMPHIS	451	398	53	11.8
MINNEAPO	492	464	28	5.7
NEWARK	308	241	67	21.8
PAWTUCK	421	375	46	10.9
PHOENIX	22	9	13	59.1
PITTSBUR	493	457	36	7.3
SEATTLE	446	376	70	15.7
TUCSON	313	241	72	23.0
UCDAVIS	381	320	61	16.0
Totals	6318	5527	791	12.5

Table 8.12
ECG Quality Grades

Clinic Name	Total ECGs	Grades					Percent Unacceptable (Grades 4-5)
		1	2	3	4	5	
Minneapolis	465	422	39	4	0	0	0.00%
Chicago	135	87	39	3	5	1	4.44%
Bettendorf	170	87	56	17	2	8	5.88%
Buffalo	365	241	84	18	8	14	6.03%
Birmingham	360	154	143	41	7	15	6.11%
UCDavis	339	162	121	32	11	13	7.08%
Brigham	341	171	118	25	8	19	7.92%
Pawtucket	388	212	119	25	6	26	8.25%
Phoenix	12	5	6	0	0	1	8.33%
Evanston	173	101	49	8	4	11	8.67%
Newark	264	143	72	26	6	17	8.71%
Iowa City	252	91	111	28	10	12	8.73%
LaJolla	355	188	105	28	9	25	9.58%
Memphis	416	242	99	34	15	26	9.86%
Atlanta	304	169	70	34	8	23	10.20%
Pittsburgh	466	221	140	47	18	40	12.45%
Bowman	331	132	107	45	13	34	14.20%
Tucson	266	82	114	30	16	24	15.04%
Seattle	402	153	136	44	24	45	17.16%
Total	5804	**3063**	**1728**	**489**	170	354	9.03%

Table 8.13

Matching Rates for Bone Scan IDs Based on Bone Scans Received at UCSF by Clinical Centers

Data as of: 08/31/94

CLINIC	Number of UCSF Scans	Number of UCSF Scans Match/w WHI Scan Forms (ID,Date)	UCSF Scans Not Match/w WHI Scan Forms	% Not Matched
BIRMING	308	292	16	5.2
PITTSBUR	512	494	18	3.5
TUCSON	546	474	72	13.2
Total	1366	1260	106	7.8

Table 8.14

Matching Rates for Bone Scan IDs Based on Bone Scans Logged Into WHILMA by Clinical Centers

(Form Cutoff Date: 08/31/94)

Data as of: 08/31/94

CLINIC	Number of WHI Scan Forms	Number of WHI Scan Forms Match/w UCSF Scans (ID,Date)	WHI Scan Forms Not Match/w UCSF Scans	% Not Matched
BIRMING	294	292	2	0.7
PHOENIX	8	0	8	100.0
PITTSBUR	502	494	8	1.6
TUCSON	499	474	25	5.0
Total	1303	1260	43	3.3

9. Adherence to Study Timeline

Protocol *Section 11* defines the study timeline, reflecting the progress and expectations as of August, 1994.

Protocol approval for study initiation was obtained from the WHI Executive Committee on July 1, 1993, from the WHI Data and Safety Monitoring Board on June 16, 1993, and from the Fred Hutchinson Cancer Research Center's Institutional Review Board on August 19, 1993. The Investigational New Drug (IND) application to the FDA was approved in July 1993. Study procedures and forms were approved in parallel. During the summer of 1993, the WHI also underwent an extensive review by the Institute of Medicine.

In spite of an initial delay of about three months in the award of the VCCs, recruitment in the WHI CT was officially opened on schedule on September 1, 1993 through the determined effort of many WHI investigators and staff. Ten VCCs were able to begin screening visits in the first month, though IRB, facilities and staffing problems, and competing study recruitment delayed screening in some VCCs until October (four VCCs) or November (two VCCs). The first randomization occurred on October 29, 1993.

The startup for the OS was delayed by the need to obtain OMB clearance for all forms, procedures, and participant materials used for OS women. The OS was officially opened for enrollment on September 1, 1994. The delay in the opening of the OS 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. This delay will result in a loss of approximately 35,200 years of observation (4% of expected).

On September 29, 1994, 24 new CCs were named. These CCs are scheduled to begin recruitment and screening in February 1995 with accrual to be completed by January 31, 1998. With each CC's recruitment goals defined on the basis of 45 CCs rather than the 40 actually funded, this will result in a deficit of 7,000 participants in the CT and over 11,000 in the OS. To address this shortfall, VCCs are being invited to make proposals to recruit beyond their currently funded levels during the period of February 1995 through January 1998.

During the next six months, VCCs will conduct their first annual follow-up visits for CT participants. The first annual visit will provide key information on study adherence and some intermediate endpoints. Enrollment into CaD, planned to occur in the 8-week window surrounding the first annual visit, will begin as soon as study medications are available. We are currently working under the assumption that these supplies will be supplied to us by December, 1994. The first CaD randomization should occur shortly thereafter.

CONFIDENTIAL

Women's Health Initiative
Clinical Trial and Observational Study

Annual Report

Volume 2: Clinical Trial Monitoring

September 1, 1993 to August 31, 1994

Prepared by
WHI Clinical Coordinating Center
Fred Hutchinson Cancer Research Center

Ross Prentice, Principal Investigator

Funded by National Institutes of Health Contract No. N01-WH-2-2110

October 3, 1994

WHI Annual Report
Volume 2
Clinical Trial Monitoring

Contents

1. Preliminary Remarks

This report documents study activities of the Women's Health Initiative Clinical Trial (CT) during the period September 1, 1993 to August 31, 1994 as reflected by data provided to the Clinical Coordinating Center (CCC) by the Vanguard Clinical Centers (VCCs, funded in Spring 1993) and the CCC subcontractors (central laboratories) by August 31, 1994. The *WHI Annual Report, Volume 2: Clinical Trial Monitoring* presents issues of particular interest to the WHI Data and Safety Monitoring Board (DSMB). Presentations include those designed to address the feasibility of the design and the safety and ethical issues of continuing the randomized Clinical Trial (CT) components as defined by the current Protocol. To protect the blinding and confidentiality of these results, the *WHI Annual Report, Volume 2* circulation is limited to the WHI DSMB and appropriate NIH and CCC staff. The reader is referred to the *WHI Annual Report, Volume 1: Study Progress* for more detailed information on study activities of a non-confidential nature.

All data presented here are derived from WHILMA, the study database, or in the case of serious adverse effects, by direct communication. Data managed in WHILMA are those defined by standardized data collection procedures and instruments (see WHI Manuals, *Volume 2 - Procedures* and *Volume 3 - Forms*). As the first Annual Report for WHI, data on many aspects are not yet complete. In some instances, simple listings are shown or sparse tables are presented to demonstrate a proposed reporting format. Other data summaries will be developed as the study and database mature.

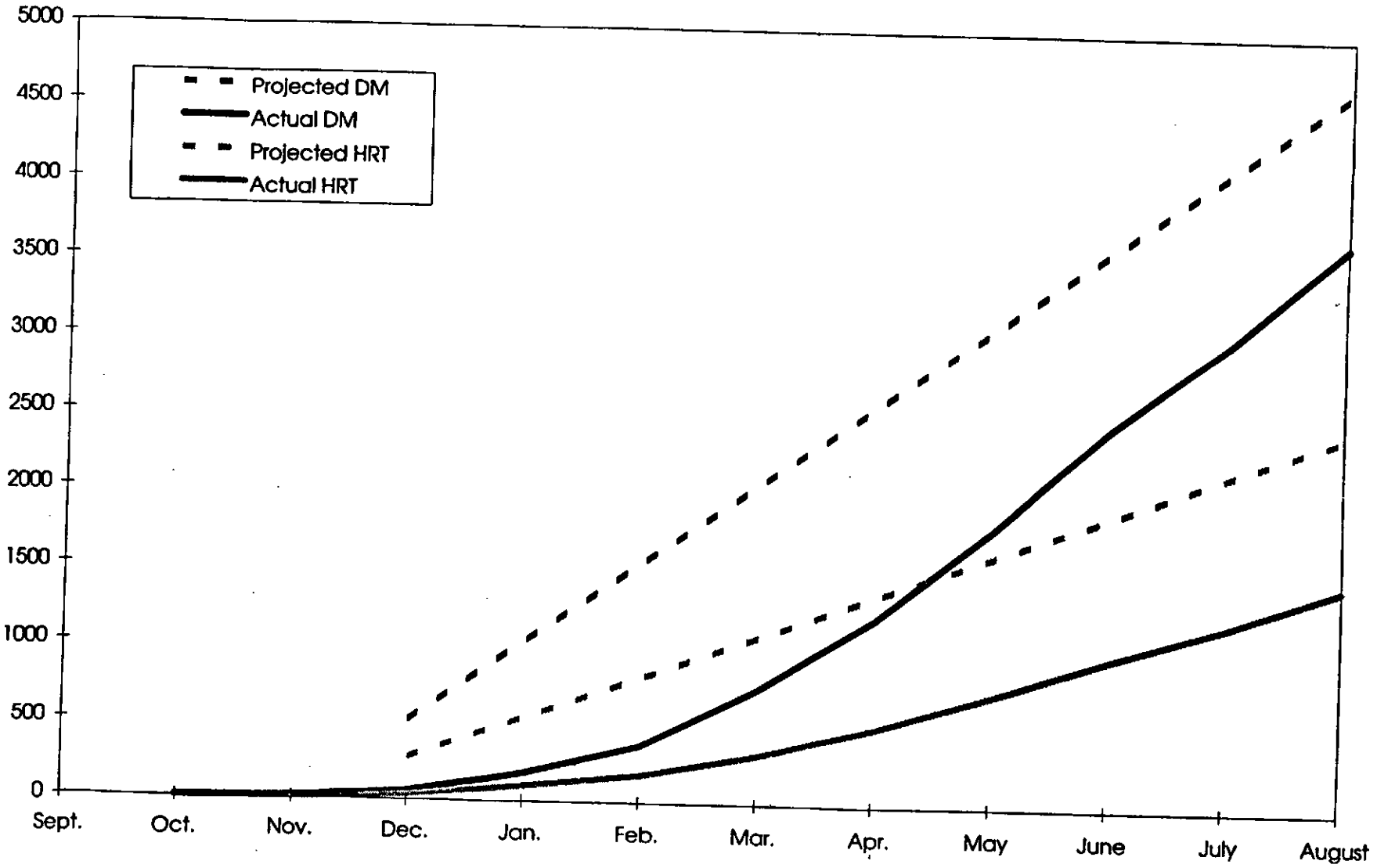
2. Enrollment

Enrollment into WHI is a multistage process consisting of recruitment, screening and randomization into the CT (or registration into the Observational Study). *Vol. 1 - Study Protocol and Policies, Protocol Section 5.2. - Enrollment* describes the model screening process. Briefly, eligibility and willingness to participate in either the Hormone Replacement Therapy (HRT) component, the Dietary Modification (DM) component, or both are determined through a series of three Screening Visits (SV1-SV3). Clinical Centers (CCs) may tailor the process to local needs, subject to the constraints of informed consent and pre-randomization data requirements. Power calculations assumed a uniform accrual during a 36-month recruitment period. For the purposes of establishing CC goals, we made the following assumptions: (1) the expected time from initial contact to SV3 would be three months; and (2) CCs should reach full accrual (randomization rates) by month 4 (December 1993 for VCCs). From these we calculated monthly goals of 16.8 HRT and 32.3 DM randomizations per month per CC or 270 HRT and 517 DM randomizations per month for all 16 VCCs.

Figure 2.1 - Projected and Actual Cumulative Randomizations by Month displays the cumulative randomizations and goals for the HRT and DM components. As of August 31, 1994 the WHI had randomized 4,496 women into the CT. Of these, 1,447 are randomized to HRT (59.6% of cumulative goal) and 3,665 are randomized to DM (78.7% of cumulative goal). While the cumulative goals have not yet been reached, *Figure 2.2. - DM and HRT Randomizations per Month* shows that monthly DM randomization goals have been exceeded for the last four months and randomizations into HRT are approaching the monthly goals (97% in August). The lag in HRT accrual is partly due to a lower than anticipated interest in the HRT component. It is also affected by a longer average screening interval associated with the HRT washout and run-in periods. If the current rate of accrual can be maintained (125% of monthly goal), the VCCs should be able to meet their cumulative goals for DM within the next year. Though VCCs have made good progress toward meeting the monthly HRT goals, additional effort will be required to cover the existing shortfall.

The randomization scheme for WHI is based on a randomized permuted block algorithm, stratified by CC site, by age category (50-54, 55-59, 60-69, 70-79) and, for HRT, by hysterectomy status. Randomization ratios are defined as 30:28:42 for ERT:PERT:placebo in HRT and 4:6 for Intervention:Control in DM. *Figure 2.3. - Randomization Assignments in the Partial Factorial Design* shows a comparison of the number expected in each cell by design (compare to *Figure 1* of the Protocol in *Vol. 1 - Study Protocol and Policies, Section 2 - Protocol*) under the current sample size and the number assigned. Of the 1,447 women randomized to HRT, 468 (32.3%) were assigned to ERT, 335 (23.2%) were assigned to PERT, and 644 (44.5%) were assigned to placebo. Of the 3,665 women randomized into DM, 1,455 (39.7%) were randomized to Intervention and 2,210 (60.3%) to Control.

Figure 2.1.
Projected and Actual HRT and DM Randomizations

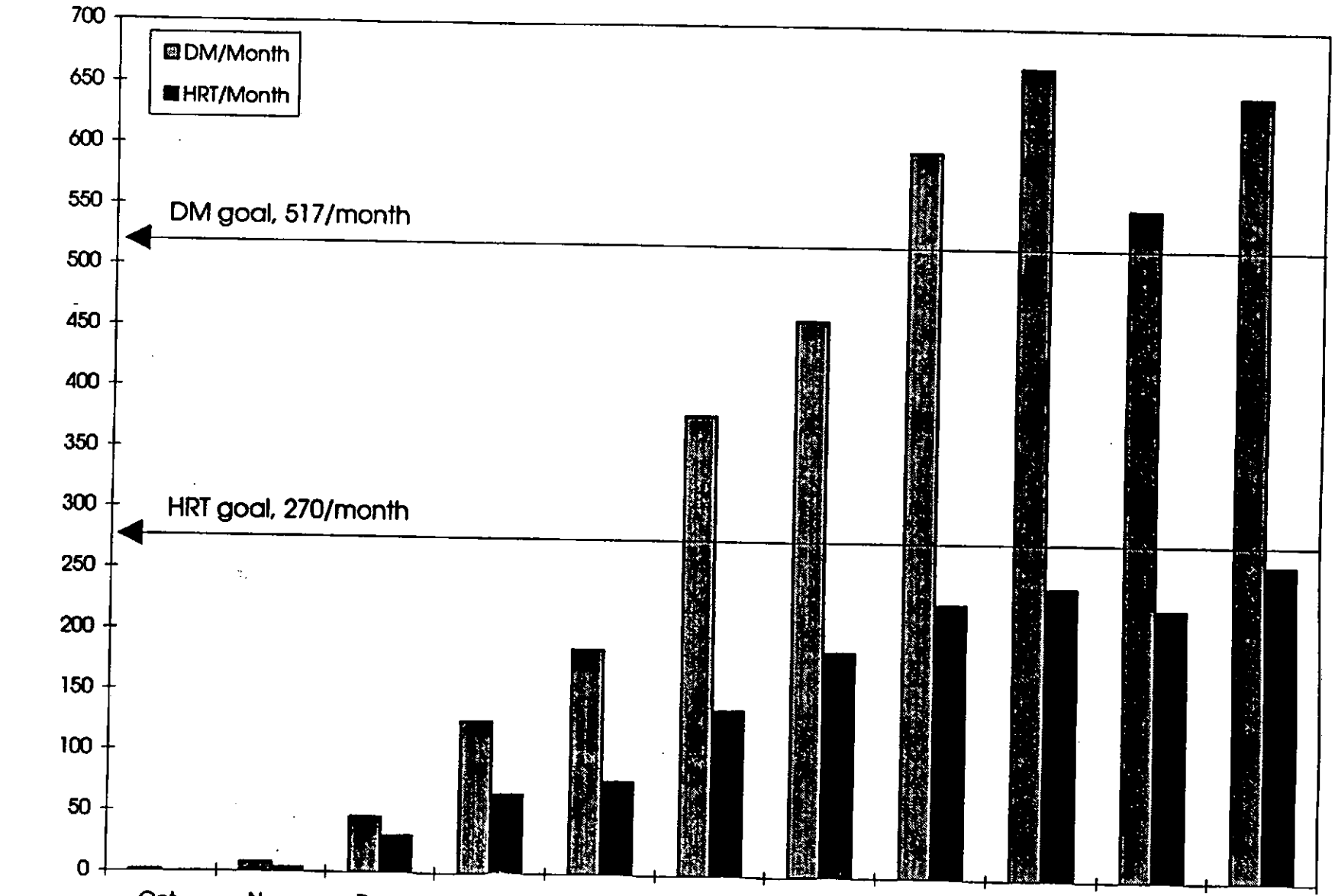


Data as of August 31, 1994

KMC1.XLS

Figure 2.2.

DM and HRT Randomizations per Month

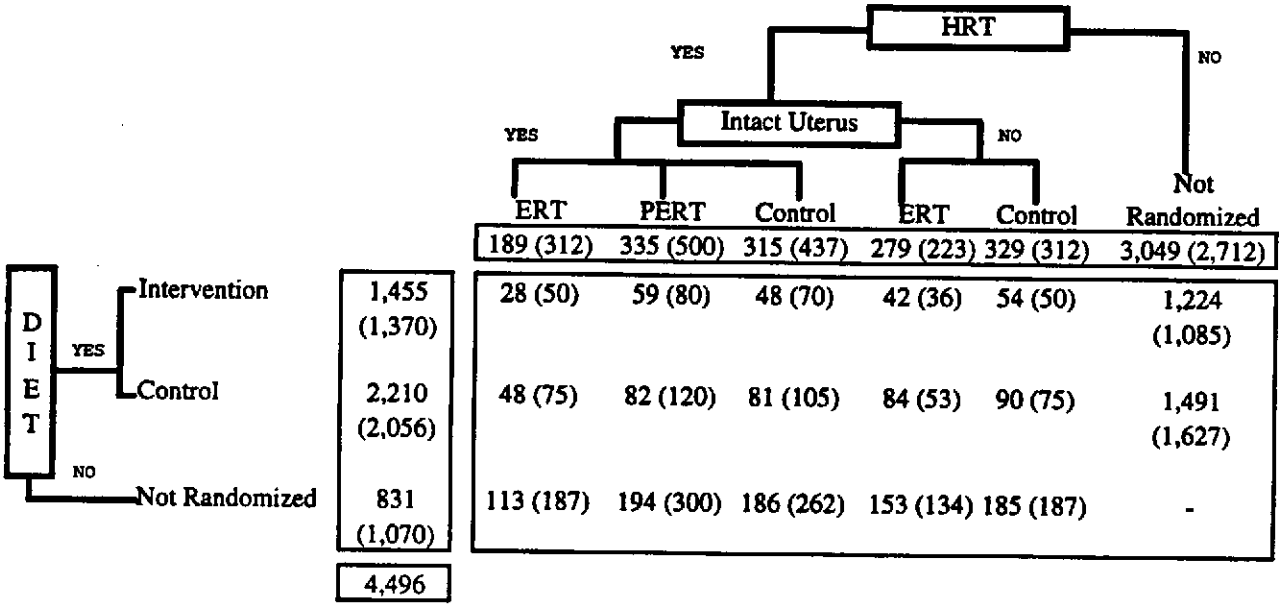


Data as of August 31, 1994

KMC1.XLS, Graph2

Figure 2.3.
Randomization Assignments in Partial Factorial Design

Number of women randomized in each cell with number projected from total sample size and design assumptions shown in parentheses.



3. Baseline Characteristics

3.1. Design Parameters and Study Goals

Age and, for HRT, hysterectomy status are design factors used in determining the required sample size for the CT. *Figure 3.1. - Age Distribution by Study Component and Hysterectomy Status* displays the current age among randomized women in each distribution component. Note that the prescribed age distribution for each 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 is to be limited to 30%.

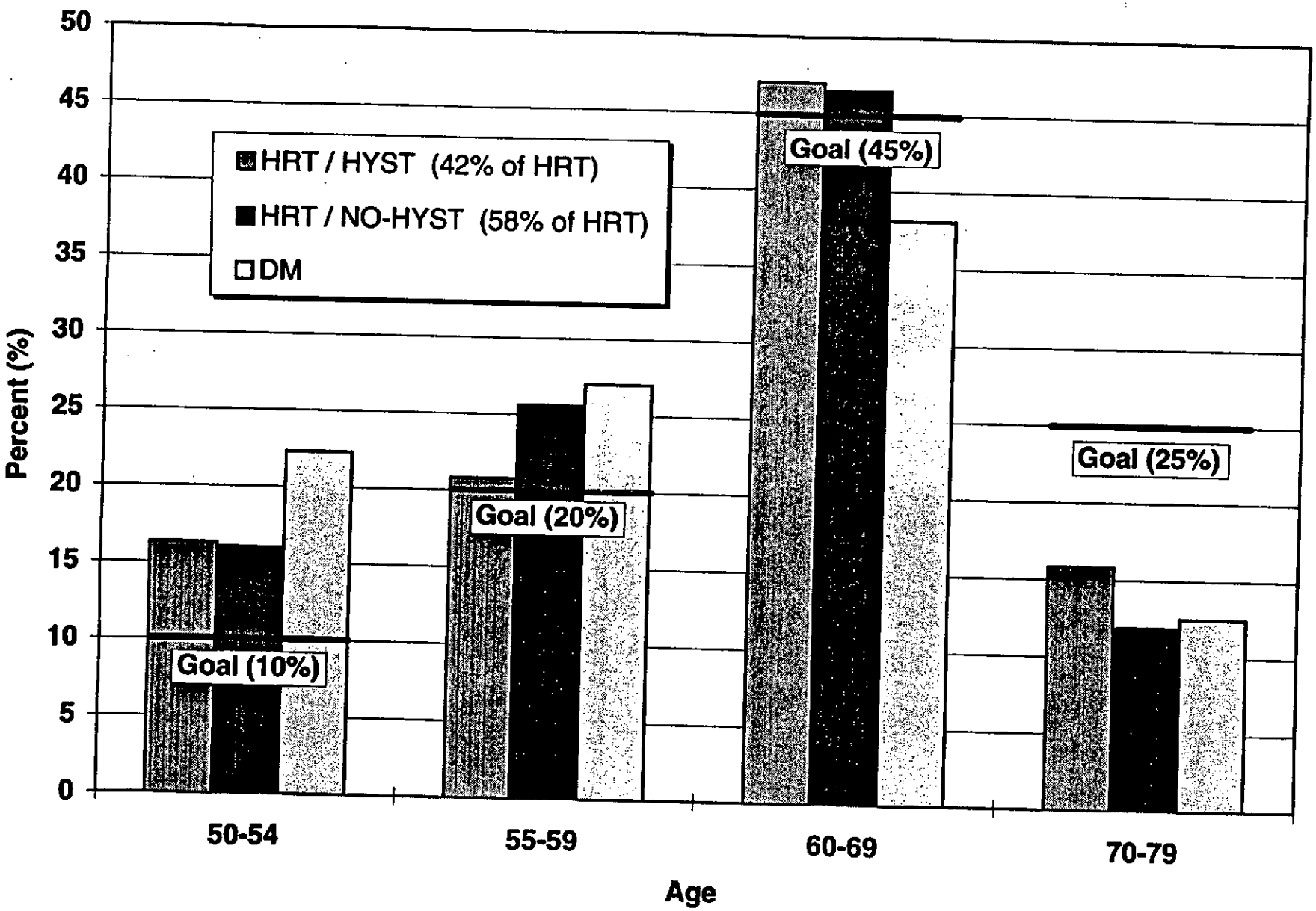
The study has a clear deficit in the oldest age category; only 13.5% of HRT participants and 12.5% of DM participants are 70-79 years of age. 42% of women randomized to HRT have had hysterectomies. While there is some variability in the degree, these trends are uniform across CCs. The lower than anticipated number of women in the oldest age range affects the power of all CT components since the largest proportion of outcomes are expected to occur in this group of women. The higher prevalence of hysterectomies at baseline affects the power of the PERT vs. Placebo comparison. Since women with hysterectomies are not randomized to PERT, a higher prevalence of hysterectomy would reduce the sample size for the PERT vs. Placebo comparison. At the August 2, 1994 Executive Committee meeting, VCCs were asked to begin targeting older women through preferential recruitment and screening of these women.

3.2. Distribution and Balance on Selected Baseline Characteristics

To demonstrate the balance achieved on other baseline characteristics, *Tables 3.1.* through *3.9. - Questionnaire Response by Randomization Assignment* present treatment arm-specific distributions for the following selected variables: race/ethnicity, marital status, income, education, ever smoker, alcohol, family history of breast cancer, parity, age at first pregnancy. *Table 3.10. - Physical Measures by Randomization Assignment* shows the treatment arm-specific distributions for height, weight, body mass index, and blood pressure.

Figure 3.1.

Age Distribution by Study Component and Hysterectomy Status



Data as of August 31, 1994

Data as of: 08/31/94

Table 3.1.
Questionnaire Responses
By Randomization Assignment

Short Verbiage	Questionnaire Response	Hormone Replacement: ERT	%	PERT	%	Placebo	%	Diet Modification: Int	%	Control	%
Racial or ethnic group	American Indian or Alaskan Native	0	0.0	0	0.0	3	0.5	5	0.3	4	0.2
	Asian or Pacific Islander	4	0.9	2	0.6	2	0.3	10	0.7	9	0.4
	Black or African-American	31	6.6	16	4.8	42	6.5	87	6.0	130	5.9
	Hispanic	24	5.1	14	4.2	22	3.4	42	2.9	61	2.8
	White	409	87.4	297	88.7	570	88.5	1300	89.3	1986	89.9
	Other	0	0.0	5	1.5	4	0.6	10	0.7	18	0.8
	Value not entered	0	0.0	1	0.3	1	0.2	1	0.1	2	0.1
	Total	468	100.0	335	100.0	644	100.0	1455	100.0	2210	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1218	2	1	105	Racial or ethnic group
2532	2	2	18	Racial or ethnic group

Data as of: 08/31/94

Table 3.2.
Questionnaire Responses
By Randomization Assignment

Short Verbiage	Questionnaire Response	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
Marital status	Never married	16	3.4	17	5.1	16	2.5	61	4.2	93	4.2
	Divorced or separated	81	17.3	43	12.9	112	17.4	185	12.7	323	14.6
	Widowed	71	15.2	50	15.0	110	17.1	181	12.4	292	13.2
	Presently married	295	63.0	215	64.4	398	61.9	1008	69.3	1464	66.3
	Living in a marriage-like relationsh	3	0.6	9	2.7	5	0.8	19	1.3	34	1.5
	Value not entered	2	0.4	0	0.0	2	0.3	1	0.1	3	0.1
	Total	468	100.0	334	100.0	643	100.0	1455	100.0	2209	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1745	20	1	25	Marital status

Table 3.3.

Questionnaire Responses
By Randomization Assignment

Data as of: 08/31/94

Short Verbiage	Questionnaire Response	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
Total family income	Less than $10,000	29	6.2	22	6.6	43	6.7	43	3.0	85	3.8
	$10,000 to $19,999	77	16.5	49	14.7	89	13.8	163	11.2	234	10.6
	$20,000 to $34,999	140	29.9	80	24.0	183	28.5	330	22.7	539	24.4
	$35,000 to $49,999	91	19.4	66	19.8	122	19.0	332	22.8	475	21.5
	$50,000 to $74,999	74	15.8	63	18.9	113	17.6	291	20.0	432	19.6
	$75,000 to $99,999	24	5.1	15	4.5	44	6.8	134	9.2	170	7.7
	$100,000 to $149,999	9	1.9	15	4.5	18	2.8	64	4.4	112	5.1
	$150,000 or more	7	1.5	8	2.4	7	1.1	34	2.3	56	2.5
	Don't know	9	1.9	7	2.1	12	1.9	32	2.2	45	2.0
	Value not entered	8	1.7	9	2.7	12	1.9	32	2.2	61	2.8
	Total	468	100.0	334	100.0	643	100.0	1455	100.0	2209	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1755	20	1	34	Total family income

Data as of: 08/31/94

Table 3.4.
Questionnaire Responses
By Randomization Assignment

Short Verbiage	Questionnaire Response	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
Highest grade in school	Didn't go to school	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
	Grade school (1-4 years)	9	1.9	5	1.5	6	0.9	3	0.2	8	0.4
	Grade school (5-8 years)	9	1.9	7	2.1	13	2.0	14	1.0	23	1.0
	Some high school (9-11 years)	37	7.9	14	4.2	24	3.7	38	2.6	64	2.9
	High school diploma or G.E.D.	96	20.5	67	20.1	146	22.7	247	17.0	399	18.1
	Vocational or training school	62	13.2	39	11.7	70	10.9	130	8.9	218	9.9
	Some college or Associate Degree	137	29.3	81	24.3	160	24.9	462	31.8	666	30.1
	College graduate or Baccalaureate	36	7.7	32	9.6	71	11.0	172	11.8	235	10.6
	Some college after college graduatio	33	7.1	39	11.7	69	10.7	173	11.9	244	11.0
	Master's Degree	42	9.0	41	12.3	73	11.4	185	12.7	319	14.4
	Doctoral Degree	5	1.1	7	2.1	10	1.6	28	1.9	31	1.4
	Value not entered	1	0.2	2	0.6	1	0.2	3	0.2	2	0.1
	Total	468	100.0	334	100.0	643	100.0	1455	100.0	2209	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1741	20	1	20	Highest grade in school

Data as of: 08/31/94

Table 3.5.
Questionnaire Responses
By Randomization Assignment

Short Verbiage	Questionnaire Response	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
Smoked 100 cigarettes	No	240	51.4	170	50.7	331	52.1	701	48.4	1106	50.5
	Yes	225	48.2	164	49.0	303	47.7	744	51.4	1080	49.3
	Value not entered	2	0.4	1	0.3	1	0.2	3	0.2	5	0.2
	Total	467	100.0	335	100.0	635	100.0	1448	100.0	2191	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
2019	34	1	8	Smoked 100 cigarettes

Data as of: 08/31/94

Table 3.6.
Questionnaire Responses
By Randomization Assignment

Short Verbiage	Questionnaire Response	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
12 alcoholic drinks ever	No	60	12.8	44	13.1	97	15.3	164	11.3	238	10.9
	Yes	407	87.2	290	86.6	538	84.7	1281	88.5	1951	89.0
	Value not entered	0	0.0	1	0.3	0	0.0	3	0.2	2	0.1
	Total	467	100.0	335	100.0	635	100.0	1448	100.0	2191	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
2039	34	1	28	12 alcoholic drinks ever

Data as of: 08/31/94

Table 3.7.
Questionnaire Responses
By Randomization Assignment

Short Verbiage	Questionnaire Response	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
Female relatives breast cancer	No	137	29.3	103	30.7	193	30.3	377	26.0	618	28.1
	Yes	74	15.8	58	17.3	82	12.9	250	17.2	348	15.8
	Don't know	7	1.5	3	0.9	8	1.3	27	1.9	36	1.6
	Value not entered	249	53.3	171	51.0	355	55.6	797	54.9	1195	54.4
	Total	467	100.0	335	100.0	638	100.0	1451	100.0	2197	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1895	32	1	89	Female relatives breast cancer

Table 3.8.
Questionnaire Response Ranges
By Study Component and Treatment Assignment

Data as of: 08/31/94

Short Verbiage	Questionnaire Response Range	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
Live births	None	7	1.5	6	1.8	15	2.3	27	1.9	43	1.9
	1	37	7.9	30	9.0	46	7.1	143	9.8	184	8.3
	2	102	21.8	72	21.5	149	23.1	364	25.0	565	25.6
	3	108	23.1	86	25.7	176	27.3	338	23.2	578	26.2
	4	79	16.9	41	12.2	105	16.3	218	15.0	325	14.7
	5	52	11.1	33	9.9	51	7.9	107	7.4	151	6.8
	6	18	3.8	16	4.8	29	4.5	72	4.9	75	3.4
	7	10	2.1	11	3.3	16	2.5	23	1.6	35	1.6
	8 or more	15	3.2	10	3.0	16	2.5	26	1.8	36	1.6
	No value entered	40	8.5	30	9.0	41	6.4	137	9.4	218	9.9
	Total	468	100.0	335	100.0	644	100.0	1455	100.0	2210	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1775	31	1	12	Live births

Data as of: 08/31/94

Table 3.9.
Questionnaire Response Ranges
By Study Component and Treatment Assignment

Short Verbiage	Questionnaire Response Ranges	Hormone Replacement						Diet Modification			
		ERT	%	PERT	%	Placebo	%	Int	%	Control	%
Age first full-term pregnancy	Less than 20	88	18.8	43	12.8	100	15.5	177	12.2	306	13.8
	20-24	209	44.7	139	41.5	286	44.4	670	46.0	939	42.5
	25-29	91	19.4	79	23.6	155	24.1	335	23.0	519	23.5
	30-34	26	5.6	24	7.2	41	6.4	74	5.1	144	6.5
	35-39	4	0.9	8	2.4	3	0.5	23	1.6	29	1.3
	40-44	0	0.0	2	0.6	0	0.0	3	0.2	0	0.0
	No value entered	50	10.7	40	11.9	59	9.2	173	11.9	273	12.4
	Total	468	100.0	335	100.0	644	100.0	1455	100.0	2210	100.0

Questionnaire Fields Used On Report

Field Id	Form	Version	Field Order	Verbiage
1773	31	1	10	Age first full-term pregnancy

Table 3.10.

Physical Measurements by Randomization Arm

	HORMONE REPLACEMENT THERAPY												DIET MODIFICATION						TOTAL		
	ESTROGEN			PROGESTIN/ESTROGEN			ESTROGEN PLACEBO			PROGESTIN PLACEBO			DIET INTERVENTION			CONTROL					
Measure	N	Mean	SE	N	Mean	SE	N	Mean	SE	N	Mean	SE	N	Mean	SE	N	Mean	SE	N	Mean	SE
WEIGHT KG	468	74.94	0.69	335	73.47	0.81	474	75.62	0.67	170	75.80	1.09	1455	75.17	0.38	2210	74.69	0.30	4496	74.39	0.21
HEIGHT CM	468	161.44	0.29	335	162.11	0.36	474	161.75	0.27	170	162.06	0.46	1455	162.38	0.16	2210	162.28	0.13	4496	162.22	0.09
BMI	468	28.73	0.25	335	27.98	0.30	474	28.91	0.25	170	28.87	0.40	1455	28.62	0.18	2210	28.38	0.11	4496	28.31	0.09
SYSTOLIC 1	468	129.94	0.80	335	127.26	0.94	474	129.58	0.84	170	129.01	1.49	1455	128.28	0.48	2210	128.24	0.38	4496	128.33	0.27
DIASTOLIC 1	468	76.91	0.42	335	76.05	0.52	474	76.97	0.43	170	77.59	0.66	1455	76.87	0.24	2210	76.64	0.20	4496	76.70	0.14

4. Follow-up Activities

4.1. Overview

Routine follow-up contacts for the CT are designed to ascertain outcomes, to assure safety, and to assess adherence to interventions. The follow-up schedule consists of telephone contacts at six weeks post-randomization for HRT, semi-annual clinic visits for HRT, semi-annual contacts (visits, telephone or mail contacts at CC discretion) for DM, and annual clinic visits for all CT women. The Protocol defines a four week interval surrounding the anniversary of randomization or surrounding six months post-randomization as the designated contact window. Completeness of follow-up is an important indicator of the adequacy of outcome ascertainment procedures. For DM, identical follow-up activities across the unblinded treatment arms is necessary to assure unbiased outcome ascertainment.

The first annual visit is the most comprehensive follow-up visit. Most baseline measures as well as the specimen collection is repeated for all CT women to provide estimates of intervention effects on intermediate endpoints. For cost efficiency, many procedures are performed throughout the follow-up period on only a subsample of participants.

4.2. Adherence to Contact Schedule

Table 4.1. - Adherence to First Semi-Annual Contact displays adherence to contact schedule for the first semi-annual contact. Data are shown only for women whose contact window was completed by August 31, 1994, indicating that a contact should have occurred. Since the first CT randomization was October 29, 1993, no annual visits are due yet. In future reports we will show follow-up activity by randomization assignment.

Adherence to contact schedule is lower than desirable overall. This represents delays in finalizing, implementing and entering the follow-up instruments, delays in scheduling follow-up visits because of anticipated protocol changes regarding follow-up, and the need to catch up on the randomization goals.

4.3. Participation Status

Women may refuse to participate in continued intervention or follow-up activities. Women who withdraw from further intervention are encouraged to participate in routine follow-up procedures to promote complete outcome ascertainment. Women who decline Protocol-defined safety-related follow-up procedures are withdrawn from the intervention. Reports of women changing their participation status post-randomization are submitted on *Form 7 - Participation Status*. Currently no data are available from this form.

Data As Of: 08/31/94

Table 4.1
Adherence to First Semi-Annual Contact by Clinical Center

Clinic	Number Due*	Number Conducted		Number Conducted In Window**	
ATLANTA	0				
BIRMING	19	15	(78.95%)	13	(68.42%)
BOWMAN	16	5	(31.25%)	1	(6.25%)
BRIGHAM	24	7	(29.17%)	7	(29.17%)
BUFFALO	37	27	(72.97%)	22	(59.46%)
CHICAGO	6	3	(50.00%)	1	(16.67%)
IOWACITY	6	6	(100.00%)	6	(100.00%)
LAJOLLA	24	6	(25.00%)	5	(20.83%)
MEMPHIS	46	37	(80.43%)	36	(78.26%)
MINNEAPO	69	66	(95.65%)	57	(82.61%)
NEWARK	4	3	(75.00%)	2	(50.00%)
PAWTUCK	15	15	(100.00%)	9	(60.00%)
PITTSBUR	27	21	(77.78%)	18	(66.67%)
SEATTLE	3	3	(100.00%)	1	(33.33%)
TUCSON	17	1	(5.88%)	1	(5.88%)
UCDAVIS	38	37	(97.37%)	27	(71.05%)
Totals	351	252	(71.79%)	206	(58.69%)

* Number Due = Members randomized 6.5 months or more ago (calculated from 'Data As Of' date)
** Number Conducted in Window = Members having a first semi-annual visit between 5.5 and 6.5 months after randomization

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 number of tablets remaining in the returned bottles and the length of the interval between visits. Changes to study medications can 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. - Medication Rates by Randomization Assignment presents adherence to study hormones by treatment arm and CC at the first semi-annual follow-up visit. In the placebo group, 94% of the prescribed tablets were consumed; for both the ERT and PERT groups, the average consumption rate was 95%. The small number of values available makes it unreasonable to draw any strong inference even for this early adherence point.

Four women have had a documented change in their study hormone prescription. These changes are listed in *Table 5.2. - Changes in HRT Medication*. In all cases except the one (involving a post-randomization hysterectomy), the clinic gynecologist was unblinded prior to changing the prescription. These changes are consistent with Protocol-defined treatment of symptoms. In two cases, the change was only to add short-term progestin to the randomized hormone assignment.

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.

Table 5.3. - Reports of Bleeding by Randomization Assignment presents the number of reports of bleeding (among women with uteri) by treatment arm and contact type. Nine women (eight PERT, one ERT) have reported bleeding at their first semi-annual visit; four PERT cases and one ERT case resulted in unblinding for management of this symptom. Among non-routine contacts, 4% of ERT and 8% of PERT are reporting bleeding problems. There have been no reports of bleeding among women on placebo. No data are yet available from the 6-week telephone contact.

5.3. Adverse Effects

There has been one adverse effect (deep vein thrombosis) reported in a 71 year old woman with a history of DVT associated with birth control pills and knee replacements. This woman had been randomized to PERT approximately six weeks prior to the event.

5.4. Unblinding

Unblinding to the HRT 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, 1994, 11 HRT participants' assignment had been unblinded. *Table 5.5. - HRT Unblindings*, provides a listing of all unblindings and relevant data. EPLC and PPLC are database variables indicating the estrogen placebo and the combined progestin plus estrogen placebo, respectively.

5.5. Laboratory Monitoring

Plans for specimen analyses to be used for monitoring purposes are currently under discussion among WHI Investigators. It is anticipated that the battery of tests to be applied to a 6% cohort of CT participants will be finalized shortly. Simultaneous analyses of baseline and year 1 samples in these women should begin by mid to late 1995. We anticipate that initial treatment group comparisons of these values will be available for our 1996 report.

Table 5.1.

MEDICATION ADHERENCE RATES

Clinic	ERT		PERT		PLACEBO	
	Members	Avg	Members	Avg	Members	Avg
ATLANTA	0		0		0	
BIRMING	2	1.01	3	0.99	6	0.95
BOWMAN	1	0.62	0		1	1.03
BRIGHAM	0		1	0.90	3	1.01
BUFFALO	5	0.99	2	0.97	3	0.97
CHICAGO	0		0		1	0.99
IOWACITY	3	0.98	2	0.87	0	
LAJOLLA	3	1.09	2	0.95	2	0.94
MEMPHIS	7	0.94	7	0.86	14	0.97
MINNEAPO	12	0.91	12	0.97	19	0.92
NEWARK	0		1	1.00	2	0.97
PAWTUCK	4	0.95	2	0.97	4	0.95
PITTSBUR	3	0.84	3	0.95	4	0.98
SEATTLE	2	0.97	1	0.94	0	
TUCSON	1	0.97	1	0.99	0	
UCDAVIS	5	0.97	5	0.98	3	0.72
Total	48	0.95	42	0.95	62	0.94

Table 5.2.
Changes in Dispensed Medications

Member ID	Medication at Randomization	Medication Exceptions: Medication Exception	Medication Exceptions: Effective Date	Medication Exceptions: Exception Reason	Open Label Dispensations: Dispensation Date	Open Label Dispensations: Dispensed Medications
16 10042 P	PERT	ERT	06/01/94	gynecologist unblinded ppt due to symptoms; prescribed switch to ERT		
21 10092 Y	ERT				06/22/94	MP10mg
					08/10/94	MP10mg
21 10218 M	PERT	ERT	06/27/94	Participant will have hysterectomy 6/29/94 - EMM.		
25 10218 Q	PERT				08/30/94	MP10mg

Table 5.3.

On Study Bleeding Summary - Year 1

Treatment Arm	6 Week Contact: Number With a Form 10	6 Week Contact: Number Bleeding	6 Week Contact: %	Semi-Annual Visit: Number With a Semi-Annual Visit	Semi-Annual Visit: Number Bleeding	Semi-Annual Visit: %	Non-Routine Contact: Number Randomized	Non-Routine Contact: Number Bleeding	Non-Routine Contact: %
ERT	0	0		20	1	5.0%	189	7	3.7%
PERT	0	0		44	8	18.2%	335	28	8.4%
Placebo	0	0		38	0	0.0%	315	0	0.0%

Table 5.4
Unblindings Report

Randomization Date	Unblind Date	Member ID	Clinic	HRT adv effects	Overdose	Medical Reason	GYN Consult	Treat without unblinding	PI Override	Reason for unblinding	Study	Arm
04/25/94	05/31/94	26 10190 M	NEWARK	Y	N	N	Y	Y	N	pt seriously depressed;tearful;unable to get out or move around	HRT	EPLC
12/01/93	12/03/93	30 10056 U	UCDAVIS	N	N	N	N	N	Y	To check for appropriate randomization	HRT	ERT
02/03/94	06/28/94	24 10353 M	MEMPHIS	Y	N	N	Y	Y	N	Abnormal bleeding	HRT	ERT
02/10/94	06/13/94	21 10092 Y	IOWACITY	Y	N	N	Y	Y	N	Excessive Bleeding	HRT	ERT
12/02/93	07/14/94	28 10043 P	PITTSBUR	Y	N	N	Y	N	Y	vaginal bleeding past 6 months	HRT	PERT
01/11/94	07/15/94	25 10065 Y	MINNEAPO	Y	N	N	Y	N	Y	bleeding at 6 months	HRT	PERT
01/11/94	07/15/94	25 10224 W	MINNEAPO	Y	N	N	Y	N	Y	bleeding at 6 months	HRT	PERT
01/31/94	07/28/94	25 10218 Q	MINNEAPO	Y	N	N	Y	N	Y	BLEEDING AT SIX MONTH VISIT	HRT	PERT
02/01/94	05/31/94	16 10042 P	CHICAGO	Y	N	N	Y	Y	N	Severe breast tenderness, persistant (but not severe) bleeding.	HRT	PERT
05/02/94	06/20/94	21 10198 P	IOWACITY	Y	N	N	Y	Y	N	has deep vein thrombosis which could be caused by HRT	HRT	PERT
07/28/94	08/30/94	23 10805 A	PAWTUCK	N	N	Y	Y	Y	Y	PRIMARY CARE PHYSICIAN REQUEST - STROKE RIGHT EYE	HRT	PERT

6. Dietary Modification Status

6.1. Timeliness of Intervention

Because the Dietary Modification (DM) intervention is delivered in a group format, the first major hurdle in conducting the DM intervention is in assigning those women randomized in the Dietary Change (intervention) arm into an intervention group. Ideally, all women in the Dietary Change arm should start intervention sessions within 12 weeks of randomization. Women waiting 20 weeks or more must be classified as minimal participants and other remedial action must be taken. See WHI Manuals, *Vol. 2 - Procedures, Section 6.10.6. - Levels of DM Intervention Participation* for further details.

Tables 6.1. - Waiting Time for Start of Intervention Among DM Intervention Participants and *6.2. - DM Participants Awaiting Intervention Start-Up* display the timeliness of initiating intervention by Clinical Center. *Table 6.1.* shows the length of time women waited between being randomized and starting intervention. Of the 1,455 women randomized to DM intervention, 781 have started intervention. Of the 781 women who have started intervention, 678 (86.8%) started within 12 weeks post-randomization. *Table 6.2.* shows the number of women waiting to start intervention. Of 1,455 DM participants randomized to the Dietary Change arm, 674 (46.3%) are awaiting group assignment and the start of intervention. Of the women awaiting intervention startup, 130 (19.3%) have been waiting 12 weeks or more and 62 (9.2%) have been waiting 16 weeks or more.

6.2. Adherence to the Intervention Program

Adherence to the DM intervention is assessed by attendance to group intervention sessions, and by self-monitoring reports of fat, fruit, vegetable, and grain scores. *Table 6.3. - Dietary Modification Session Adherence Summary* displays the study-wide reports of session attendance and completion (where completion equals group attendance plus make-up attendance), and the average of the self-monitoring scores by session.

Table 6.4. - Percent of Participants Completing Dietary Sessions displays session attendance for each Vanguard Clinical Center.

Attendance study-wide ranges from 97.8% at session 1 to 93.2% at session 7 to 90.4% at session 10 (*Table 6.3.*). Sessions move from weekly to biweekly at session 7 and from biweekly to monthly at session 10. Experience from the Women's Health Trial suggests that attendance will decline when the time interval between sessions becomes longer. Note that scores have not been recorded yet for session 10 pending a change in data recording procedures. This accounts for the low member count for scores at session 10.

The study-wide average fat gram score declined from 47.4 at session 2, when participants begin turning in their fat scores, to 26.8 at session 8 when participants are expected to have met their fat gram goals. Assigned fat gram goals range from 29-37, with 32-34 being most frequently assigned. Fat gram goals are individually defined in *Vol. 1 - Study Protocol and Policies, Protocol Section 4.2.2.* from participant height and baseline total energy intake. The CCC monitors fat scores at sessions 8, 12, and 16, with the expectation that participants should have attained their fat gram goals by session 8. Fat scores are collected and recorded

at each session beginning with session 3 so that participants and nutritionists can track progress toward the goal.

The study-wide average fruit/vegetable score was 5.6 servings at session 8 when participants begin turning in their fruit/vegetable scores. This score is already above the DM intervention goal of 5 fruit/vegetable servings daily. Data (member count for scores) are insufficient to evaluate beyond session 9. The CCC monitors fruit/vegetable scores at sessions 12 and 16, with the expectation that participants should have attained their fruit/vegetable goals by session 12. Participants turn in fruit/vegetable scores beginning with session 8 so that they and their nutritionists can track progress toward their goals.

The study-wide average grain score was 4.7 at session 8 when participants begin turning in their grain scores. This score is below the DM intervention goal of six servings daily. Data (member count for scores) are insufficient to evaluate beyond session 9. The CCC monitors grain scores at session 16, with the expectation that participants should have attained their grain goals by session 16. Participants turn in their grain scores beginning with session 8 so that they and their nutritionists can track progress toward their goals.

6.3. Number of Active Groups and Group Sizes

The number of active groups and group sizes are displayed in *Table 6.5. - Number of DM Intervention Women Assigned to Diet Groups at Session 01*. Seventy groups are active, i.e., participants have been assigned to a group. All VCCs have conducted at least one group through session 6. One VCC has conducted at least one group through session 13. No VCCs have conducted session 14 or beyond.

The recommended group size is 8-15 participants, with the ideal range being 10-12 participants. Groups that are too small may lead to staff overload. Groups that are too large lead potentially to poor group dynamics. Forty-four percent of the groups are in the ideal size range. One VCC has two groups that are smaller than the recommended size. One VCC has one group that is larger than the recommended size.

6.4. Comparison of Dietary Intake

Dietary intake in DM is assessed at baseline and post-randomization in both the Intervention and Comparison arms with three instruments: the *FFQ*, the *4DFR*, and the 24 Hour Recall (*24HR*). Currently only baseline values of the *FFQ* are available.

6.5. Laboratory Monitoring of Adherence to Dietary Intervention Program

Plans for specimen analyses to be used for monitoring purposes are currently under discussion among WHI Investigators. It is anticipated that the battery of tests to be applied to a 6% cohort of CT participants will be finalized shortly. Simultaneous analyses of baseline and year 1 samples in these women should begin by mid to late 1995. We anticipate that initial treatment group comparisons of these values will be available for our 1996 report.

Table 6.1

Women's Health Initiative
Waiting Time for Start of Intervention Among DM Intervention Participants
By Clinical Center

Data as of: 08/31/94

Clinic Name	Randomized to DM/INT	Intervention Started	Pct Total	time from randomization to intervention startup: < 4 Weeks	Pct Total	4-<8 Weeks	Pct Total	8-<12 Weeks	Pct Total	12-<16 Weeks	Pct Total	16+ Weeks	Pct Total
ATLANTA	68	24	35.3	6	25.0	6	25.0	9	37.5	2	8.3	1	4.2
BIRMING	97	31	32.0	6	19.4	12	38.7	6	19.4	3	9.7	4	12.9
BOWMAN	90	41	45.6	11	26.8	14	34.1	12	29.3	3	7.3	1	2.4
BRIGHAM	109	49	45.0	28	57.1	13	26.5	4	8.2	3	6.1	1	2.0
BUFFALO	95	55	57.9	18	32.7	26	47.3	6	10.9	2	3.6	3	5.5
CHICAGO	77	41	53.2	12	29.3	15	36.6	8	19.5	3	7.3	3	7.3
IOWACITY	83	21	25.3	4	19.0	5	23.8	5	23.8	6	28.6	1	4.8
LAJOLLA	89	55	61.8	9	16.4	16	29.1	12	21.8	7	12.7	11	20.0
MEMPHIS	103	69	67.0	30	43.5	26	37.7	8	11.6	3	4.3	2	2.9
MINNEAPO	125	76	60.8	23	30.3	29	38.2	13	17.1	9	11.8	1	1.3
NEWARK	64	37	57.8	13	35.1	11	29.7	9	24.3	2	5.4	1	2.7
PAWTUCK	99	75	75.8	14	18.7	24	32.0	24	32.0	10	13.3	3	4.0
PITTSBUR	81	62	76.5	30	48.4	20	32.3	9	14.5	2	3.2	0	0.0
SEATTLE	122	69	56.6	22	31.9	30	43.5	12	17.4	4	5.8	1	1.4
TUCSON	60	9	15.0	3	33.3	3	33.3	2	22.2	0	0.0	1	11.1
UCDAVIS	93	67	72.0	24	35.8	28	41.8	8	11.9	5	7.5	2	3.0
Totals	1455	781	53.7	253	32.4	278	35.6	147	18.8	64	8.2	36	4.6

Table 6.2

Women's Health Initiative
DM Participants Awaiting Intervention Startup
By Clinical Center

Data As Of: 08/31/94

Clinic Name	Randomized to DM/INT	Awaiting DM Intervention	Pct Total	time since randomization: < 4 Weeks	Pct Total	4-<8 Weeks	Pct Total	8-<12 Weeks	Pct Total	12-<16 Weeks	Pct Total	16+ Weeks	Pct Total
ATLANTA	68	44	64.7	2	4.5	14	31.8	8	18.2	8	18.2	12	27.3
BIRMING	97	66	68.0	2	3.0	22	33.3	19	28.8	13	19.7	10	15.2
BOWMAN	90	49	54.4	2	4.1	16	32.7	16	32.7	13	26.5	2	4.1
BRIGHAM	109	60	55.0	1	1.7	13	21.7	14	23.3	16	26.7	16	26.7
BUFFALO	95	40	42.1	3	7.5	13	32.5	12	30.0	8	20.0	4	10.0
CHICAGO	77	36	46.8	1	2.8	9	25.0	9	25.0	7	19.4	10	27.8
IOWACITY	83	62	74.7	7	11.3	13	21.0	12	19.4	13	21.0	17	27.4
LAJOLLA	89	34	38.2	1	2.9	10	29.4	10	29.4	6	17.6	7	20.6
MEMPHIS	103	34	33.0	1	2.9	15	44.1	11	32.4	5	14.7	2	5.9
MINNEAPO	125	49	39.2	0	0.0	16	32.7	18	36.7	9	18.4	6	12.2
NEWARK	64	27	42.2	0	0.0	16	59.3	5	18.5	3	11.1	3	11.1
PAWTUCK	99	24	24.2	0	0.0	8	33.3	8	33.3	6	25.0	2	8.3
PITTSBUR	81	19	23.5	2	10.5	4	21.1	9	47.4	3	15.8	1	5.3
SEATTLE	122	53	43.4	2	3.8	11	20.8	5	9.4	16	30.2	19	35.8
TUCSON	60	51	85.0	2	3.9	14	27.5	12	23.5	11	21.6	12	23.5
UCDAVIS	93	26	28.0	2	7.7	18	69.2	5	19.2	1	3.8	0	0.0
Totals	1455	674	46.3	28	4.2	212	31.5	173	25.7	138	20.5	123	18.2

Data As Of: 08/31/94

Table 6.3

Dietary Modification Session Adherence Summary

Session ID	Members Assigned	Members Evaluated	Attended Session	Completed Session	Percent Complete	---Fat Scores--- Member Count	Average Grams	---F/V Scores--- Member Count	Average Servings	--Grain Scores-- Member Count	Average Servings
01	810	781	697	764	97.82	1	0.0	0		0	
02	759	708	626	689	97.32	43	47.4	0		0	
03	710	649	568	630	97.07	534	33.7	0		0	
04	667	640	549	620	96.88	595	30.4	0		0	
05	618	579	500	562	97.06	514	28.6	0		0	
06	579	517	433	491	94.97	451	27.3	0		0	
07	539	425	351	396	93.18	370	26.6	8	5.4	8	3.9
08	494	357	282	331	92.72	310	26.8	300	5.6	300	4.7
09	324	266	213	251	94.36	231	26.3	225	5.6	225	4.5
10	232	115	91	104	90.43	4	26.4	4	5.0	4	4.2
11	133	69	52	62	89.86	56	24.1	56	6.7	56	4.9
12	59	21	17	19	90.48	17	24.7	17	5.2	17	5.3
13	10	10	8	8	80.00	7	27.4	7	5.9	7	5.5
14	0	0	0	0	0.00	0		0		0	
15	0	0	0	0	0.00	0		0		0	
16	0	0	0	0	0.00	0		0		0	
17	0	0	0	0	0.00	0		0		0	
18	0	0	0	0	0.00	0		0		0	
19 (Individual)	324	182	0	182	100.00	169	26.8	169	5.8	169	4.6

Table 6.4

Percent of Participants Completing Dietary Sessions
By Clinical Center

Clinic Name	DIETARY INSTRUCTIONAL SESSIONS 01	02	03	04	05	06	07	08	09	10	11	12	13
ATLANTA	100.00	100.00	100.00	100.00	100.00	83.33							
BIRMING	90.32	87.10	88.89	90.32	100.00	88.89	91.67						
BOWMAN	95.12	95.00	100.00	96.67	93.33	95.24	100.00	95.00	100.00	88.89	77.78		
BRIGHAM	100.00	100.00	100.00	97.96	100.00	100.00	97.96	100.00	87.76				
BUFFALO	100.00	100.00	96.36	98.18	96.36	94.55	92.73	85.37	92.31	88.46	81.82	81.82	
CHICAGO	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	87.50	87.50			
IOWACITY	100.00	100.00	100.00	100.00	100.00	100.00	77.78						
LAJOLLA	94.55	98.11	96.15	94.23	96.55	93.10	82.76	75.00					
MEMPHIS	100.00	98.51	95.65	100.00	100.00	97.01	100.00	100.00	100.00	100.00	95.00		
MINNEAPO	100.00	98.68	100.00	100.00	98.48	96.23	94.34	92.11	96.55	77.78	94.74	100.00	80.00
NEWARK	100.00	100.00	100.00	100.00	95.45	100.00	87.50	100.00					
PAWTUCK	94.67	95.24	98.00	94.34	92.86	100.00	96.55	89.66	96.55				
PITTSBUR	100.00	95.08	92.98	98.18	96.36	98.15	96.55	93.10	93.10	93.33			
SEATTLE	92.75	97.62	95.24	92.86	92.86	90.00	82.35	88.89	85.71				
TUCSON	100.00	100.00	88.89	88.89	88.89	77.78	77.78	66.67					
UCDAVIS	100.00	97.01	97.01	96.36	97.67	93.02	88.37	100.00	100.00	94.74	90.00		

Table 6.5

Number of DM Intervention Women Assigned to Diet Groups at Session 01
By Clinical Center

Clinic Name	Number of Groups	Number of Women Assigned in Each Group At Session 01									
		<8 Women	Pct Total	8-9 Women	Pct Total	10-12 Women	Pct Total	13-15 Women	Pct Total	>15 Women	Pct Total
ATLANTA	2	0	0.0	0	0.0	2	100.0	0	0.0	0	0.0
BIRMING	2	0	0.0	0	0.0	0	0.0	1	50.0	1	50.0
BOWMAN	6	0	0.0	0	0.0	6	100.0	0	0.0	0	0.0
BRIGHAM	4	0	0.0	0	0.0	2	50.0	2	50.0	0	0.0
BUFFALO	4	0	0.0	0	0.0	1	25.0	3	75.0	0	0.0
CHICAGO	4	0	0.0	2	50.0	1	25.0	1	25.0	0	0.0
IOWACITY	2	0	0.0	1	50.0	1	50.0	0	0.0	0	0.0
LAJOLLA	4	0	0.0	0	0.0	1	25.0	3	75.0	0	0.0
MEMPHIS	6	0	0.0	1	16.7	4	66.7	1	16.7	0	0.0
MINNEAPO	7	0	0.0	2	28.6	3	42.9	2	28.6	0	0.0
NEWARK	3	0	0.0	1	33.3	0	0.0	2	66.7	0	0.0
PAWTUCK	7	0	0.0	3	42.9	2	28.6	2	28.6	0	0.0
PITTSBUR	6	2	33.3	0	0.0	2	33.3	2	33.3	0	0.0
SEATTLE	6	0	0.0	0	0.0	1	16.7	5	83.3	0	0.0
TUCSON	1	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0
UCDAVIS	6	0	0.0	1	16.7	5	83.3	0	0.0	0	0.0
Totals	70	2	2.9	12	17.1	31	44.3	24	34.3	1	1.4

7. Outcomes

7.1. Overview

Outcomes are ascertained at all routine follow-up visits. Initial reports of clinical outcomes are obtained on *Form 33 - Medical History Update* or through routine procedures during the annual visit (e.g., mammography, endometrial aspirations, ECGs). Depending on the type, outcomes may be accepted based on self-report, or local and central adjudication may be required. WHI Manuals, *Vol. 2 - Procedures, Section 17 - Outcomes* for further details.

7.2. Initial Report of Outcomes

As of August 31, 1994, *Form 33 - Medical History Update* data were available for 312 women. Among these, 32 women reported hospitalizations since randomization. Self-reported new diagnoses included: heart/circulatory problems (n=2); cancer (n=1); stroke/TIA (n=1). In the future, we will tabulate initial reports of clinical outcomes by outcome type, study component, and treatment arm.

7.3. Confirmed Outcomes

No outcomes have been confirmed. Documentation and adjudication awaits implementation of outcomes procedures currently under development. In the future, we will tabulate confirmed clinical outcomes by outcome type, study component, and treatment arm, and make comparisons based on the proposed monitoring scheme, as appropriate.

8. Study Design and Power

CT power calculations were based on assumptions involving the accrual rate, 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, Protocol Section 2-3A*) for more details. *Table 8.1. - Design Assumptions and Current Estimates* summarizes the observable quantities that we monitor. As noted in earlier sections, the data are not adequate yet to provide useful estimates of factors related to follow-up.

The lag in accrual and the under-recruitment of women aged 70-79 and of women with intact uteri have been presented and discussed among WHI Investigators. It is still anticipated that the original goals can be met. Current priorities are to address first the lag in recruitment on a clinic-by-clinic basis and then to work on subgroup goals, hopefully by January 1995.

Because the observed deviances from design parameters are believed to be correctable, the projected power of these studies has not been noticeably affected by deviances to date. We will present updated power calculations when indicated by any substantial deviation from current assumptions.

Table 8.1.
Design Assumptions and Current Estimates

	Parameter	Design Value	Current Estimate for HRT	DM
Accrual Rate	Average follow-up	8.92 yrs.	8.86 [1]	8.9 [1]
Baseline Characteristics	% randomized as			
Age	50-54	10%	16.1%	22.3%
	55-59	20%	23.6%	27.1%
	60-69	45%	46.7%	38.1%
	70-79	25%	13.5%	12.5%
Hysterectomy Status	Intact Uterus	70%	58%	
	Hysterectomized	30%	42%	
Loss to Follow-up/ Competing Risk	Event rate (%/year)		no data available	
	CHD	2%		
	All others	3%		
Outcomes	Incidence Rates among Control Group			
Breast Cancer	(%/year)	0.355% [2]	no data available	
Colon Cancer		0.160% [2]		
CHP		0.294% [2]		
Hip Fractures		0.258% [2]		

[1] Assumes monthly goals will be met in all remaining months and that deficits will be filled by September 1995.

[2] These values represent the expected incidence among control women during the early years of the study. Age effects and secular trends are incorporated in the design for selected outcomes.

Table 8.1. (Cont.)
Design Assumption and Current Estimates

Adherence	Parameter	Design Value		Current Estimate for	
		Intervention	Control	Intervention	Control
DM Intervention	% cal from fat				
	Baseline	38	38	no data available	
	Year 01	21.7	37.8		
	Year 02	22.6	37.2		
	Year 10	26	34		
HRT	% changing arms Active to Control				
	Year 1	6%			
	Years 2-10	3%/year			
	Control to Active				
	Years 1-5	1.5%/year			
	Years 6-10	1%/year			

9. Ancillary Studies

The WHI Ancillary Study policy defines an ancillary study as an investigation which is not described in the WHI Protocol and involves additional data which are not collected as part of the routine WHI data set, or additional biologic specimens for analysis or storage. Separate informed consent must be obtained on all ancillary study participants. Every ancillary study is initially sent to the Design and Analysis Subcommittee for review. The purpose of the Design and Analysis Subcommittee review is to assure that the ancillary study does not unduly: (1) interfere with the objectives of WHI or complicate the interpretation of results; (2) result in unblinding the study interventions: (3) adversely affect participant burden or cooperation in the WHI; or (4) jeopardize the public image of the WHI. In particular, ancillary studies involving randomization assignments for CT women generally need to wait until completion of pertinent CT components before randomized treatment group comparisons can be done. The Executive Committee may also request the review and approval of the WHI Data and Safety Monitoring board. See WHI Manuals *Vol. 1 - Study Protocol and Policies, Section 3.4.* for a complete statement of the Ancillary Study policy.

Table 9.1 - WHI Ancillary Studies lists all proposals received by the Design and Analysis Subcommittee and the approval status as determined by that Subcommittee. No ancillary study has yet been referred to the DSMB for review.

Table 9.1.
Ancillary Study Proposal Tracking

Study ID#	TITLE	Study's Principal Investigator	Initiating Clinical Center	D&A Approval	Total # of Participating Clinics	Study Population	Sample Size
AS1	ADAPT	John Crouse	Bowman Gray	Conditional	5	DM	
AS2	PLCO Cancer Screening Trial	Joel Weissfeld	Pittsburgh	Disapproved	1	OS	2,200
AS3	PLCO Offer to WHI-Partners	Joel Weissfeld	Pittsburgh	Conditional	?	Partners	
AS4	Clinical Prostate Cancer	Catarina Kiefe	Birmingham	Concept	2	DM Partners	
AS5	Explanations for the Development of Fat Distaste	Pamela Green	Seattle	Conditional	1	DM	160
AS6	Symptomatic Musculoskeletal Disease in Older Women	Susan Hughes	Chicago	Approved	1	OS	
AS7	HRT and Cardiovascular Morbidity and Mortality - Low Ankle/Arm BPI	Lewis Kuller	Pittsburgh	Approved	7	HRT	12,714
AS8	Partner's Health Study	Robert Langer	LaJolla	Approved	1	Partners	1,500
AS9	Osteoporosis and Oral Bone Loss	Cora E. Lewis	Birmingham	Approved	1	OS	1,000
AS10	Urinary Estrogen Metabolites and Breast Cancer Risk	Elaine Meilahn	Pittsburgh	Conditional	4	DM	80,000
AS11	Validation and Exploration of Sleep and Mood Predictors	Daniel Kripke	LaJolla	Approved	1	OS	
AS12	Empowerment/Nutritional Counseling	Charles Mouton	Newark	Disapproved	1	CT	
AS13	Prevalence and Correlates of lumbar spinal stenosis	Lewis Kuller	Pittsburgh	Pending a Vote	1	OS	150
AS14	High Density Lipoprotein Metabolism	Tamsen Bassford	Tucson	Conditional	1	CT & OS	200
AS15	Osteopenia and Periodontitis	Jean Wactawski-Wende	Buffalo	Conditional	1	CT & OS	2,000
AS16	Peripheral Vascular Disease	Mary McDermott	Chicago	Pending a Vote	7	OS, 65+	5,500