Women's Health Initiative
Clinical Trial and Observational Study

Semi-Annual Progress Report
August 26, 1999 to February 29, 2000

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WHI Semi-Annual Progress Report

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Executive Summary

This report summarizes data accumulated through February 29, 2000 for the three clinical trial components and the observational study component of the Women's Health Initiative (WHI). With recruitment completed, the primary areas described in this report are adherence to the interventions, participation in follow-up data collection and outcomes.

The Hormone Replacement Therapy (HRT) component completed accrual with 27,348 women randomized, including nearly 40% who had previously experienced a hysterectomy. The average follow-up on these women is just over 3 years. The proportion of women who have stopped intervention has been larger than projected in the first two years (approximately 10% per year). Subsequent drop-out rates, now with estimates available through the fifth year, have been close to design assumptions (5-7% per year). These data predate the DSMB recommended HRT update and therefore do not reflect any impact of this activity on adherence. Symptom reporting is relatively stable after the second year, with 8% or fewer of women with a uterus reporting bleeding and 3% of women reporting breast changes. Analyses of a small sample of blood specimens and bone mineral density taken at baseline and selected follow-up times are presented by hysterectomy strata. Vital status is known within the last 18 months for all but 757 women (2.8%). We lack recent follow-up on another 0.1%. Event rates for the primary outcome of CHD are currently 55% of design assumptions. Event rates for all monitored outcomes are presented by age and racial/ethnic group. Revised calculations incorporating current estimates for adherence and control group event rates, indicate that the power to test the CHD hypothesis for estrogen and for estrogen/progestin is now approximately 63% and 76%, respectively.

Recruitment into the Dietary Modification (DM) component finished with 48,837 women randomized (102% of goal). The primary intervention, delivered in group sessions over a one year period, is complete. The current focus is on the quarterly maintenance sessions and options for boosting adherence. The difference between the Intervention and Control arms in FFQ percent energy from fat (C-I) is 11%, 10.1%, 9.7%, 8.9% and 8.5% at years 1 through 5, respectively. The corresponding design assumptions for the C-I comparisons were 13% at year 1, diminishing by 0.25% per year. Multiple efforts are underway to boost and support the C-I for the remaining follow-up period. Analyses of a small sample of blood specimens and bone mineral density are presented from baseline and selected follow-up times. Vital status is known within the last 18 months for all but 1,394 women (2.9%). An additional 0.1% have not provided outcome information recently. The average follow-up time for DM women is approximately 3.25 years. Observed invasive breast cancer and colorectal cancer incidence rates are near design assumptions (80%). Event rates by age and racial/ethnic group are presented for all monitored outcomes. Using the observed values of the key parameters, the projected power for detecting a 14% reduction in breast cancer incidence is 67%, assuming a lower bound for C-I of 9% and an average of 8.5 years of follow-up. The corresponding estimated power would be 73% and 87% if a C-I of 10% could be maintained.

Randomizations into the Calcium and Vitamin D (CaD) component, designed to occur at a CT participant's first annual follow-up visit, have reached 36,102. Only a few additional women are expected to be accrued over the next few months. Adherence to CaD supplements, though still lower than desirable (55%-63% consuming at least 80% of assigned dose), has continued to show improvement in the last six months. Analyses of bone density measures are shown at the first and

third annual visit at all three skeletal sites. Follow-up rates for CaD participants are better than for the other CT components; only 1.1% have unknown vital status and 0.7% have not provided recent outcomes data. The average follow-up time in CaD is approximately 2 years. Hip fracture incidence rates are currently much lower than projected (30% of design) suggesting a strong healthy volunteer effect. Event rates by age and racial/ethnic group are presented for all monitored outcomes. With these updated parameter values and a projected average follow-up of 7.5 years, the power to detect a 27% reduction in hip fracture rates is 75%. The power for combined fractures remains high (above 99%).

Observational Study (OS) recruitment ended in December 1998 with 93,721 women participating. The average follow-up time is about 2.5 years. Follow-up activities for OS women are conducted primarily through mailed questionnaires, except at the 3-year anniversary of enrollment when a visit is required. Completeness of follow-up ranges from 91% to 96% for mailed questionnaires. The 3-year visit completeness rate is approximately 85%. Lost-to-follow-up or stop follow-up rates are low (combined value of 2.5%). Outcomes data are considered up-to-date for 91.5% of OS participants. Current event rates are shown by age and racial/ethnic groups for all routinely reported hospitalized outcomes.

The timeliness and completeness of local outcomes processing is a continuing area of focus and concern. The improvements made previously have been maintained and progress in reducing the backlog continues, but the increasing event rates create a demanding load. The recent focus has been on completing the documentation of deaths and in assuring up-to-date information on vital status. A summary of locally and centrally adjudicated outcomes and the corresponding agreement rate are also provided.

A brief summary of the Performance Monitoring Committee activities is presented. The status of papers and ancillary studies, as currently known to the Publications and Presentations and the Design and Analysis Committees is also included. Updates to these tables are needed and should be sent to the CCC.

1. Preliminary Remarks

This report documents study activities of the Women's Health Initiative (WHI) Clinical Trial (CT) during the period from August 26, 1999 to February 29, 2000, as well as the cumulative experience. Topics include continuing recruitment into the Calcium and Vitamin D (CaD) trial, and for all CT components, follow-up, intervention monitoring, safety, outcomes, study power, and specialized scientific efforts. Updates are provided for each study component separately with a separate section on outcomes devoted to data quality, processing and timeliness issues.

During this period, major milestones, emphases, and changes have included:

- Planning and implementation of the DSMB recommendation to inform HRT women of an early increased risk of cardiovascular disease,
- Full implementation of a motivational interviewing protocol to improve adherence to the DM intervention.
- Conceptual development and review of a "Tailored Message Campaign" to be implemented in the DM Intervention after the completion of the motivational interviewing protocol.
- Preparation for a clinic staff workshop to be held in May 2000 that will focus on safety monitoring and adherence in the HRT and CaD trial components, including aspects of motivational interviewing.
- Further development and implementation of global strategies to improve adherence, including such activities as sending a letter of appreciation from Dr. Lenfant, Director of NHLBI to all CT women.
- Continued recruitment into the CaD trial including randomizations through the second year of follow-up.
- Continuing efforts to assure timely and complete outcomes ascertainment.
- Completion of the first combined CT and OS "vital status sweep".
- Development of guidelines and procedures for access to and analysis of biologic specimens as initiated by the Genetics and Biomarkers Taskforce.
- Substantial effort to prepare and analyze the full baseline dataset for publishing in a special edition of the Annals of Epidemiology.

All reports summarize Clinical Center (CC) data provided to the CCC by February 29, 2000. 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

Abbreviation	CC Institution and Location	Principal Investigator
Vanguard Clinical Centers (VCCs):		
ATLANTA	Emory University Atlanta (Decatur), Georgia	Nelson Watts, MD
BIRMING	University of Alabama at Birmingham Birmingham, Alabama	Albert Oberman, MD MPH
BOWMAN	Bowman Gray School of Medicine Winston-Salem(Greensboro), North Carolina	Electra Paskett, PhD
BRIGHAM	Brigham and Women's Hospital Boston (Chestnut Hill), Massachusetts	Joann Manson, MD DrPH
BUFFALO	State University of New York, Buffalo Buffalo, New York	Maurizio Trevisan, MD MS
CHICAGO	Northwestern University Chicago and Evanston, Illinois	Philip Greenland, MD
IOWACITY	University of Iowa Iowa City and Bettendorf, Iowa	Robert Wallace, MD
LAJOLLA	University of California, San Diego La Jolla and Chula Vista, California	Robert Langer, MD MPH
MEMPHIS	University of Tennessee Memphis, Tennessee	Karen Johnson, MD
MINNEAPO	University of Minnesota Minneapolis, Minnesota	Richard Grimm, MD
NEWARK	University of Medicine and Dentistry Newark, New Jersey	Norman Lasser, 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	Shirley Beresford, PhD
TUCSON	University of Arizona Tucson and Phoenix, Arizona	Tamsen Bassford, MD
UCDAVIS	University of California, Davis Sacramento, California	John Robbins, MD

Table 1.1 (continued)
Database Abbreviations for WHI CCs

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

Table 1.1 (continued)
Database Abbreviations for WHI CCs

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

2. HRT Component

2.1 Recruitment

Recruitment into the HRT component, completed in October of 1998, reached 27,348 women (99.4% of goal). Of these, 10,739 women had a prior hysterectomy (39%) and were randomized to either unopposed estrogen (ERT) or placebo in equal proportions. The remaining 16,609 women with an intact uterus were randomized to combined estrogen/progestin (PERT) or its placebo, again in equal proportions for most of the recruitment period. *Table 2.1* documents the age distribution of this population.

2.2 Adherence

Women randomized to HRT are required to come for a clinic visit six and twelve months after randomization and annually thereafter. Adherence to medications is determined at all visits by weighing returned bottles if available or by self-report in the small proportion of women with missed pill collection. Symptoms and outcomes are also ascertained at these visits. Telephone contacts or visits are also required on the anniversary of each woman's six month visit. These contacts (or visits) serve mostly to assure safety, address possible adherence and retention issues, ascertain outcomes and promote bonding. Adherence data from telephone contacts are limited, so adherence data reported here are based on pill collections at required clinic visits.

Table 2.2 – HRT Adherence Summary gives descriptive data on all women who are considered due for each listed clinic visit. Rates of visits conducted, visits within window, stopping intervention and taking protocol-assigned medications are shown for each interval for which we have adherence data. Only summary information across arms is provided for visits that were complete in the last report. For stopping intervention and medication rates we excluded the 331 who were moved from ERT to PERT in early 1995 after our protocol change since their experience is unique in the trial. The final column is the adherence summary, our primary measure for monitoring adherence. It is defined as the number of women known to have consumed more than 80% of their assigned HRT pills during that interval as a proportion of the number randomized and eligible for this visit. 77% of women are known to be adherent at AV-1, 69% are adherent at AV-2 and only 56% by AV-5. Women with a uterus appear to be somewhat more adherent to study pills than hysterectomized women. There have been no noteworthy changes in adherence measures since the last report.

Table 2.3 presents estimated drop-in and drop-out rates based on observed data and the associated design assumptions. The design assumptions underestimated the observed values to date, particularly for the first two years of follow-up. The power calculations assumed that 6% of HRT women would stop intervention in the first year with an additional 3% per year thereafter. An independent assumption of 3% per year lost to follow-up or competing risk events gives an overall drop-out rate of 8.8% in year 1, and 5.9% per year thereafter. Our lifetable estimates of the AV-1 drop-out rates are 10.0% in hysterectomized women and 9.8% in women with a uterus. For AV-2 the estimates are 10.1% and 8.9%. Estimates for later years range from 5.0% to 7.8%. The cumulative drop-out rate for AV-5 is 34.3% for hysterectomized women and 31.6% for women with a uterus, compared to a design assumption of 28.5% for each.

The design assumed that a small proportion (1.5% per year) of the HRT participants would stop study hormone pills and begin taking hormones outside of the trial. Among hysterectomized women on placebo the observed rate is approximately 2.9% at AV-1 and 7.2% at AV-3. In women with a uterus assigned to placebo, the "drop-in" rate was 2.1% at AV-1 and 5.9% at AV-3.

In this report, we have replaced the logistic regression models that were used to examine adherence during specific visit intervals since randomization with a Cox proportional hazard model that looks at adherence over the entire follow-up period available (*Table 2.4*). This failure time model considers a woman to be non-adherent at the first visit where she took < 80% of her study pills, stopped HRT medications or was lost to follow-up. The hazard ratio estimates the risk of becoming non-adherent. Study subject and program characteristics are included as explanatory variables. In the with uterus group, reports of bleeding are collected at each visit. The effect of bleeding on adherence is represented in the model by a time-dependent covariate.

The factors related to non-adherence are similar in the two strata (with and without uterus). Women in the oldest age group are less adherent, as are blacks and Hispanics, and those who reported prior hormone use. In the with uterus strata, women reporting bleeding are less likely to be adherent. Women who completed the HRT washout and those receiving the six week phone call have better adherence.

Table 2.5 summarizes the frequency of reported reasons for stopping interventions by hysterectomy status. For all women "health problems or symptoms from the WHI intervention" is the most frequently reported reason for stopping HRT study pills. A large proportion of women who have stopped intervention report health-related problems not directly associated with the intervention or conflicts between the study and their health needs or the guidance given to them by their provider.

2.3 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. Breast tenderness is not collected regularly on all participants after AV-1. Reports of bleeding and breast changes by contact type and treatment arms are shown in *Tables 2.6* and *2.7*, respectively. Reports of bleeding in women with a uterus reached a high of 29% at 6 months (SAV-1) and have since fallen to about 8% or less after AV-3. Reports of breast changes seem to be hovering at about 3% after AV-1.

2.4 Safety Monitoring

Table 2.8 presents results of endometrial aspirations by time since randomization and study arm. As routine post-randomization biopsies are required of only a small sample (6%) of women at AV-3, AV-6, and AV-9, the vast majority of these tests represent non-routine aspirations performed in response to bleeding problems. *Table 2.8* combines the results from both protocol defined and non-routine procedures. Among 3,353 biopsies, 80 (2.4%) yielded an abnormal result: 48 cystic, 10 adenomatous, 18 atypia and 4 cancer.

2.5 Laboratory Studies

Table 2.9 presents the results of blood specimens analyses from a small (8.6%) cohort of HRT women selected randomly at baseline for these prospective analyses. This subsample incorporated over-sampling of minorities. The results shown here are weighted to reflect the overall WHI-CT distribution of race/ethnicity.

2.6 Intermediate Outcomes

Bone mineral density (BMD) measures are collected at the three BMD clinical centers (Pittsburgh, Birmingham, and Tucson) at baseline and at follow-up years 1,3,6, and 9. These data, shown in *Table 2.10*, suggest small increases in BMD between baseline and AV-1 or AV-3, with the largest change in the BMD of the spine, followed by hip and whole body. The pattern of changes is similar in both strata (with and without a uterus).

2.7 Vital Status

Table 2.11 presents data on the vital status and the participation status of participants in the HRT trial. A detailed description of CCC and clinic activities to actively locate participants who do not complete their periodic visits is given in *Section 5 – Outcomes.* For operational purposes, we define CT participants to have an "unknown" participation status if there is no outcomes information from the participant for 18 months, and no other contacts for 6 months. Currently about 2.8% of the HRT participants are lost-to-follow-up or have stopped follow-up, and 1.3% of the participants are known to be deceased. Virtually all of the remaining participants have completed a *Form 33 – Medical History Update* in the last 18 months. The design assumed that 3% per year would be lost to follow-up or death. Currently the average follow-up for HRT participants is about 3.1 years, suggesting that approximately 9.0% could be expected to be dead or lost to follow-up. Our overall rates compare favorably to design assumptions. Follow-up in women with a uterus is slightly better than hysterectomized women.

2.8 Outcomes

Table 2.12 contains counts of the number of locally verified major WHI outcomes for HRT participants by age and ethnicity. Approximately 10-15% of the self-reported outcomes have not yet been verified so the numbers in this table can be seen as a lower bound of the actual number of outcomes that have occurred. Compared to the design assumptions, we have observed about 70-75% of the expected number of CHD event, breast cancers, and colorectal cancers, and about 35% of the expected number of hip fractures. We anticipate that these percentages will increase as the "healthy volunteer effect" is diluted with time.

Table 2.13 compares the rates of the same locally verified outcomes between women who have and who have not been hysterectomized. For most cardiovascular outcomes the event rates are slightly larger for the women without a uterus, while for most cancers the rates are slightly larger for women with a uterus. Many of these differences are small and based few events. The differences in cardiovascular disease rates are consistent with the risk profile differences we have previously observed, however.

Table 2.14 contains counts of the number of self-reports for some outcomes that are not locally verified in WHI. As most of the self-reported outcomes are somewhat over-reported (see *Section 6.3 – Outcomes Data Quality*), the numbers in this table should be taken as an upper bound on the number of events that have occurred in HRT participants.

2.9 Power Considerations

The power under the design assumptions for adherence and overall incidence rates and values derived from the observed data are shown in *Table 2.15*. These calculations assume 7% drop-outs in years 1 and 2 and 4% per year through the remaining follow-up (independent of the 3% lost-to-follow-up rates) and 2.5% drop-ins per year throughout follow-up. CHD incidence rates were adjusted to reflect the lower rates observed in the early follow-up period. In addition to the 33% reduction for healthy volunteer effect that the design assumed throughout follow-up, incidence rates in years 1, 2, and 3 were further reduced by 67%, 50% and 37% respectively. These changes produced a power for the ERT vs. Placebo comparison on CHD rates of 63% compared to the design value of 81%. For the PERT comparison the power drops from 88% to 76%.

2.10 Issues

In response to the DSMB recommendation, on March 31, WHI Clinical Centers were to begin mailing an HRT update to HRT participants, informing them of the finding of a small increased risk in heart disease, stroke and blood clots in the legs and lungs during the first 2 years of the trial. This effort has been the major focus of study investigators and staff with regard to the HRT trial. Materials for participants, their physicians, staff and investigators were prepared so that the message could be distributed accurately, uniformly and efficiently. In developing these materials, many questions have arisen regarding that have bearing upon the future of this trial. Of primary concern is our ability to retain women in the study in the face of this information.

Currently, though the information is only anecdotal, the response of WHI participants has been modest and mostly positive. Clinical Centers have not reported any mass flight and only one case of an angry participant (who had experienced an event) has been reported to the CCC. In a few instances, this event has created an opportunity to re-engage women who had stopped blinded study pills so that they could take the hormones prescribed by their doctor. The plan to meet with each woman face-to-face is thought to be an excellent opportunity to further bond with these women and provide them with encouragement regarding the importance of this trial. We will be monitoring the response to this action over the next few months to gauge its effects on study integrity.

A workshop is planned in May 2000 for key clinic staff related to HRT and CaD concerns. The agenda will provide them additional information and training for boosting adherence and for safety monitoring.

Other steps have been taken to address adherence and retention challenges. In February, Clinical Centers were provided with a letter signed by Dr. Claude Lenfant, thanking WHI participants for their efforts. These mailings were to be done by the local Clinical Centers. Additional items under consideration by an Adherence and Retention Task Force led by Dr. Sally Shumaker, include increasing the frequency of the newsletters and providing additional gift/incentives.

Table 2.1
Hormone Replacement Therapy Component Age – Specific Recruitment

Data as of: February 29, 2000

	Total Randomized	% of Overall Goal	Age Distribution	Design Assumption
HRT (Overall)	**27,348**			
50-54	3426	125%	13%	10
55-59	5402	99%	20%	20
60-69	12364	100%	45%	45
70-79	6156	90%	23%	25
HRT without Uterus	**10,739**			
50-54	1398	114%	13%	10
55-59	1910	78%	18%	20
60-69	4851	88%	45%	45
70-79	2580	84%	24%	25
HRT with uterus	**16,609**			
50-54	2028	135%	12%	10
55-59	3492	116%	21%	20
60-69	7513	111%	45%	45
70-79	3576	95%	22%	25

Table 2.2
HRT Adherence Summary

Data as of: February 29, 2000

Contact	Due N	Conducted N	Conducted %	Conducted in Window N	Conducted in Window %	Stopped HRT during interval N	Stopped HRT during interval %	Missed Pill Collection N	Missed Pill Collection %	Total with Collections N	Total with Collections %	Medication Rate[1] <50% N	Medication Rate[1] <50% %	Medication Rate[1] 50%-80% N	Medication Rate[1] 50%-80% %	Medication Rate[1] 80% + N	Medication Rate[1] 80% + %	Adherence Summary[2] %
Semi-Annual Visit-1	27348	26691	98	22782	83	1405	5	1457	5	25520	95	1033	4	1905	8	22582	89	84
Annual Visit-1	27348	26493	97	21880	80	1315	5	1410	6	23759	94	1017	4	2065	9	20677	87	77
Annual Visit-2	24805	23363	94	18769	76	2276	9	2205	10	19154	90	664	4	1813	10	16677	87	69
Without Uterus	9751	9068	93	7276	75	979	10	969	12	7489	89	248	3	797	11	6444	86	67
With Uterus	15054	14295	95	11493	76	1297	9	1236	10	11665	90	416	4	1016	9	10233	88	70
Annual Visit –3	15948	14803	93	11676	73	1129	7	1066	9	11198	91	413	4	1063	10	9722	87	63
Without Uterus	6322	5785	92	4555	72	484	8	467	10	4414	90	149	3	479	11	3786	86	61
With Uterus	9626	9018	94	7121	74	645	7	599	8	6784	92	264	4	584	9	5936	88	65
Annual Visit –4	7689	7099	92	5532	72	447	6	397	7	4970	93	181	4	435	9	4354	88	60
Without Uterus	3083	2806	91	2193	71	199	7	166	8	1997	92	71	4	187	9	1739	87	57
With Uterus	4606	4293	93	3339	72	248	6	231	7	2973	93	110	4	248	8	2615	88	62
Annual Visit –5	2871	2643	92	2152	75	130	5	130	8	1603	93	62	4	142	9	1399	87	56
Without Uterus	1209	1097	91	896	74	65	6	64	8	724	92	29	4	79	11	616	85	52
With Uterus	1662	1546	93	1256	76	65	5	66	7	879	93	33	4	63	7	783	89	60

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

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

Note: Deceased women are excluded from all medication adherence calculations, but are included in the number "Due."

Table 2.3
HRT Drop-Out and Drop-In Rates by Follow-Up Time
(Design-specified values in parentheses)

Data as of: February 29, 2000

	Without Uterus				With Uterus				Overall Total			
	Interval[1]		Cumulative[2]		Interval		Cumulative		Interval		Cumulative	
Drop-Outs[3]												
AV-1	10.0%	(8.8)	10.0%	(8.8)	9.8%	(8.8)	9.8%	(8.8)	9.8%	(8.8)	9.8%	(8.8)
AV-2	10.1%	(5.9)	19.1%	(14.2)	8.9%	(5.9)	17.8%	(14.2)	9.4%	(5.9)	18.3%	(14.2)
AV-3	7.8%	(5.9)	25.4%	(19.2)	7.0%	(5.9)	23.5%	(19.2)	7.3%	(5.9)	24.3%	(19.2)
AV-4	6.6%	(5.9)	30.4%	(24.0)	5.9%	(5.9)	28.1%	(24.0)	6.2%	(5.9)	29.0%	(24.0)
AV-5	5.5%	(5.9)	34.2%	(28.5)	5.0%	(5.9)	31.6%	(28.5)	5.2%	(5.9)	32.7%	(28.5)
Drop-Ins[4]												
AV-1	2.9%	(1.5)	2.9%	(1.5)	2.1%	(1.5)	2.1%	(1.5)	2.4%	(1.5)	2.4%	(1.5)
AV-3	4.4%	(2.9)	7.2%	(4.4)	3.9%	(2.9)	5.9%	(4.4)	4.1%	(2.9)	6.4%	(4.4)

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

[2] Estimates of cumulative rates

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

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

Table 2.4
Cox Proportional Hazards Model Analysis of HRT Medication Adherence: Time to First Non-Adherent Visit [1,2]

Data as of: February 29, 2000

	HRT (N=27017)					
	Without Uterus (N=10740)			With Uterus (N=16277)		
	Non-Adherent Participants[3] (N=5191)	Adherent Participants (N=5549)	Hazard Ratio for non-adherence	Non-Adherent Participants[3] (N=7077)	Adherent Participants (N=9200)	Hazard Ratio for non-adherence
Age:						
50-54[4]	777	620	1.00	946	1031	1.00
55-59	980	934	1.01	1480	1937	1.00
60-69	2190	2662	0.98	3018	4333	1.07
70-79	1244	1333	1.11 *	1633	1899	1.30 **
Ethnicity:						
White	3591	4494	1.00	5640	8011	1.00
Black	1004	613	1.49 **	638	463	1.42 **
Hispanic	416	235	1.32 **	517	360	1.21 **
Other Minority	180	207	1.09	282	366	1.16 *
Education:						
0-8 Yrs	1503	1642	0.94	1703	2179	0.85
Some H.S./Diploma	3431	3736	0.93	5094	6827	0.82 *
Post H.S.	200	129	1.00	223	149	1.00
Income:						
<20K	1485	1368	1.00	1585	1558	1.00
20-35K	1398	1601	0.95	1788	2428	0.88 **
35-50K	880	1067	0.91 *	1307	1951	0.84 **
>50K	1077	1238	0.95	1971	2794	0.89 **
DM Randomized:						
No	3519	3829	1.00	5009	6741	1.00
Yes	1672	1720	0.92 **	2068	2459	1.03
HRT Washout:						
No	4518	4637	1.00	6598	8429	1.00
Yes	673	912	0.85 **	479	771	0.88 *
Marital Status:						
Married	2800	3186	1.00	4058	5675	1.00
Not Married	2354	2338	1.01	2979	3502	1.04
Hormones Ever:						
No	1989	2098	1.00	4183	5613	1.00
Yes	3202	3451	1.10 **	2894	3587	1.11 **
6 wk phone call						
No	420	241	1.00	531	382	1.00
Yes	4771	5308	0.85 **	6546	8818	0.80 **
On-Study bleeding[5]						
No Bleeding				4710	6855	1.00
Any Bleeding after Baseline				1805	2337	1.13 **

[1] Excludes ERT to PERT participants.

[2] * P-value <=.05 from Wald test.
** P-value <=.01 from Wald test

[3] Non-adherent in this table is defined as participants who took less than 80% of HRT medications, stopped intervention, or were lost to follow-up during any follow-up interval.

[4] Underlined levels are reference categories

[5] Included as a time-dependent covariate in model.

Table 2.5
Reasons for Stopping HRT

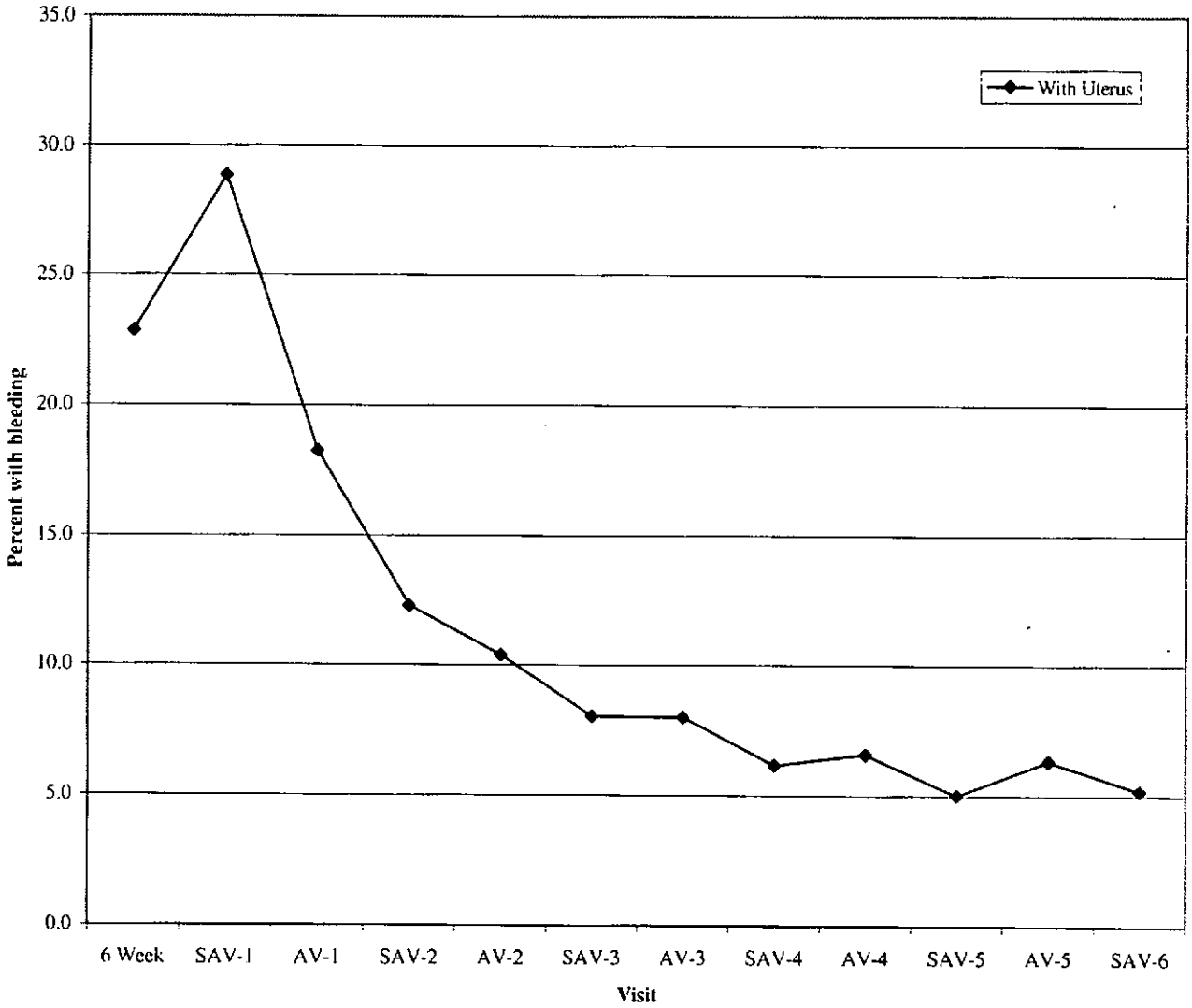
Data as of February 29, 2000

Reasons[1]	Without Uterus (N =3114)		With Uterus (N =4456)	
Personal	237	(8%)	282	(6%)
Travel	149	(5%)	142	(3%)
Study Procedures	58	(2%)	88	(2%)
Health	1356	(44%)	1705	(38%)
Experiencing health problems or symptoms not due to intervention	530	(17%)	622	(14%)
Worried about health effects of medical tests	12	(<1%)	18	(<1%)
Worried about costs if adverse effects occur	10	(<1%)	5	(<1%)
Advised not to participate by health care provider	588	(19%)	805	(18%)
Study conflicts with health care needs	543	(17%)	674	(15%)
Expected more care	9	(<1%)	14	(<1%)
Intervention	735	(24%)	1421	(32%)
Reports health problems or symptoms from WHI intervention	551	(18%)	1148	(26%)
Problem with Clinic Practitioner or other CC staff	3	(<1%)	14	(<1%)
Doesn't like taking pills	80	(3%)	94	(2%)
Doesn't like DM requirements	1	(<1%)	6	(<1%)
Problems with DM group nutritionist or group members	1	(<1%)	3	(<1%)
Doesn't like DM eating patterns	1	(<1%)	3	(<1%)
Doesn't like randomized nature of intervention	71	(2%)	105	(2%)
Expected some benefit from intervention	34	(1%)	38	(1%)
Won't participate in safety procedures.	50	(2%)	68	(2%)
Other	990	(32%)	1404	(32%)
Not Given	320	(10%)	501	(11%)

[1] Multiple reasons may be reported for a woman

Table 2.6
Reports of Bleeding

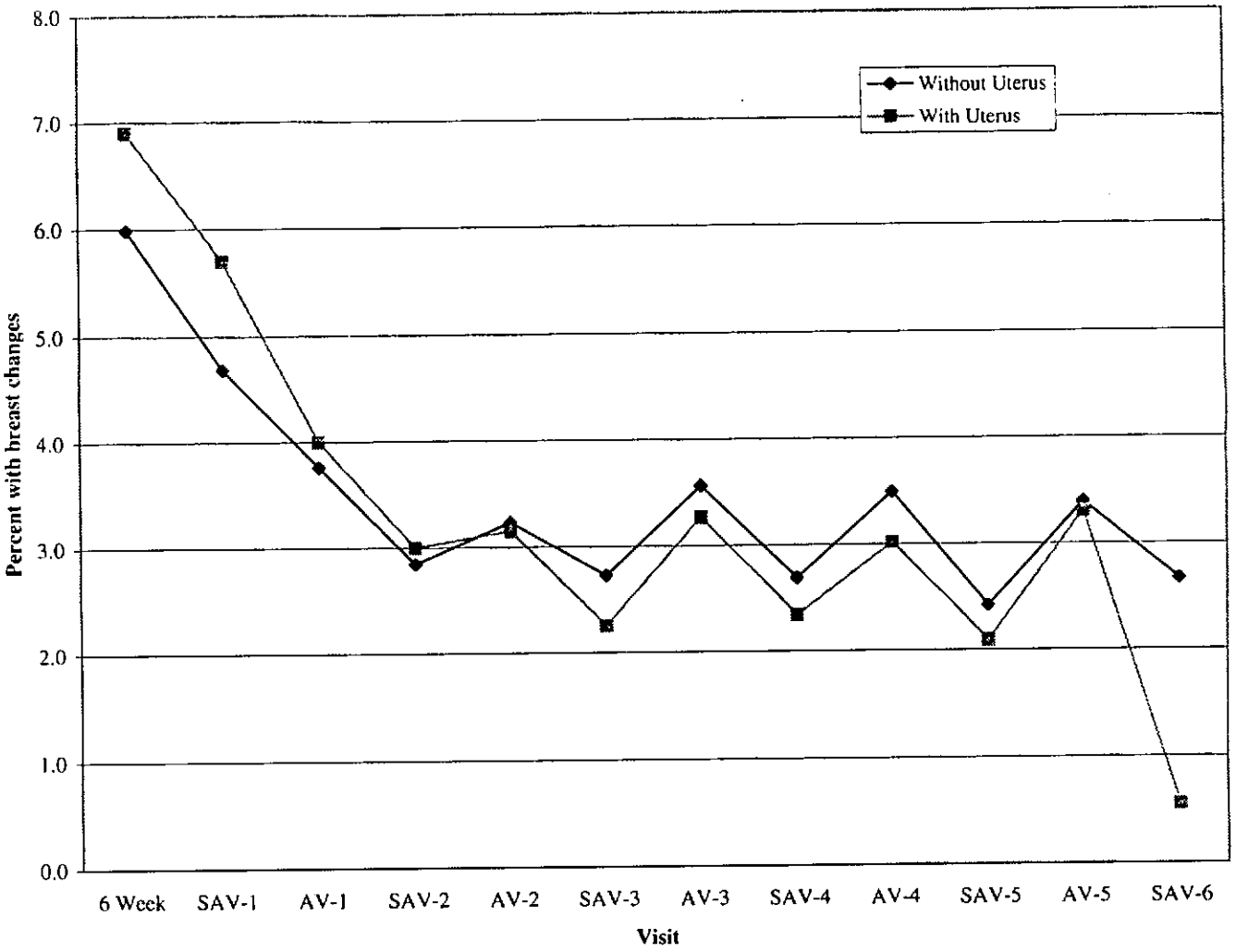
Data as of: February 29, 2000



Contact	With Uterus	
6 Week HRT Phone Call – Number with Bleeding	3579	(22.9%)
Semi-Annual Visit 1 – Number with Bleeding	4691	(28.9%)
Annual Visit 1 – Number with Bleeding	2948	(18.3%)
Semi-Annual Visit 2 – Number with Bleeding	1929	(12.3%)
Annual Visit 2 – Number with Bleeding	1485	(10.4%)
Semi-Annual Visit 3 – Number with Bleeding	940	(8.0%)
Annual Visit 3 – Number with Bleeding	721	(8.0%)
Semi-Annual Visit 4 – Number with Bleeding	382	(6.2%)
Annual Visit 4 – Number with Bleeding	282	(6.6%)
Semi-Annual Visit 5 – Number with Bleeding	131	(5.0%)
Annual Visit 5 – Number with Bleeding	98	(6.3%)
Semi-Annual Visit 6 – Number with Bleeding	36	(5.2%)

Table 2.7
Reports of Breast Changes

Data as of: February 29, 2000



Contact	Without Uterus	With Uterus
6 Week HRT Phone Call – Number with Breast Changes	603 (6.0%)	1078 (6.9%)
Semi-Annual Visit 1 – Number with Breast Changes	468 (4.7%)	900 (5.7%)
Annual Visit 1 – Number with Breast Changes	373 (3.8%)	628 (4.0%)
Semi-Annual Visit 2 – Number with Breast Changes	260 (2.8%)	432 (3.0%)
Annual Visit 2 – Number with Breast Changes	266 (3.2%)	411 (3.1%)
Semi-Annual Visit 3 – Number with Breast Changes	176 (2.7%)	229 (2.3%)
Annual Visit 3 – Number with Breast Changes	175 (3.6%)	253 (3.3%)
Semi-Annual Visit 4 – Number with Breast Changes	87 (2.7%)	119 (2.3%)
Annual Visit 4 – Number with Breast Changes	77 (3.5%)	105 (3.0%)
Semi-Annual Visit 5 – Number with Breast Changes	32 (2.4%)	43 (2.1%)
Annual Visit 5 – Number with Breast Changes	28 (3.4%)	40 (3.3%)
Semi-Annual Visit 6 – Number with Breast Changes	10 (2.7%)	3 (0.6%)

Table 2.8
Endometrial Aspiration Results

Data as of: February 29, 2000

Months since randomized	N of aspirations[2,3]	Number with Abnormal Results[1]				
		Cystic	Adenomatous	Atypia	Cancer	Total[4]
0-6	105	5	1	1	-	2
6-12	716	11	2	4	-	6
12-18	702	12	3	3	3	9
18-24	493	13	4	3	-	7
24-36	324	2	-	1	-	1
36-42	427	-	-	3	1	4
42-48	333	2	-	2	-	2
48-54	119	2	-	1	-	1
54-60	68	-	-	-	-	-
60-66	42	1	-	-	-	-
66-72	17	-	-	-	-	-
72-78	6	-	-	-	-	-
78-84	1	-	-	-	-	-
Total	3353	48	10	18	4	32

[1] Abnormal results are based on local readings with the following groupings defined as follows:
Cystic is cystic hyperplasia without atypia
Adenomatous is adenomatous hyperplasia without atypia
Atypia is atypia or cystic or adenomatous hyperplasia with atypia

[2] All endometrial aspirations after first adenomatous or worse result removed. If participants had more than one endometrial aspiration within a 30-day period, the latest was used. Please note that routine aspirations for the Endometrial Aspiration subsample are included in this table.

[3] ERT-TO-PERT removed.

[4] Row totals combine adenomatous, atypias and cancer categories

Table 2.9
Blood Specimen Analysis: HRT Participants

Data as of: February 29, 2000

	Without Uterus			With Uterus		
	N	Mean*	S.D.*	N	Mean*	S.D.*
Micronutrients						
Alpha-Carotene (µg/ml)						
Baseline	790	0.08	0.06	997	0.09	0.07
AV-1	786	0.07	0.04	997	0.08	0.06
AV-1 - Baseline	785	-0.01	0.05	996	-0.01	0.04
Alpha-tocopherol (µg/ml)						
Baseline	790	15.94	5.55	997	16.23	6.32
AV-1	786	17.44	7.55	998	16.52	5.91
AV-1 - Baseline	785	1.47	5.14	997	0.29	4.97
Beta-Carotene (µg/ml)						
Baseline	789	0.29	0.18	997	0.34	0.29
AV-1	785	0.26	0.20	998	0.30	0.24
AV-1 - Baseline	784	-0.04	0.19	997	-0.04	0.17
Beta-Cryptoxanthine (µg/ml)						
Baseline	790	0.08	0.04	997	0.09	0.06
AV-1	786	0.07	0.04	997	0.08	0.05
AV-1 - Baseline	785	0.00	0.03	996	-0.01	0.05
Gamma-tocopherol (µg/ml)						
Baseline	790	2.40	1.40	997	2.30	1.14
AV-1	786	2.14	1.67	998	1.92	1.00
AV-1 - Baseline	785	-0.27	1.01	997	-0.38	0.80
Lycopene (µg/ml)						
Baseline	790	0.40	0.16	997	0.41	0.16
AV-1	786	0.39	0.15	998	0.40	0.15
AV-1 - Baseline	785	-0.01	0.14	997	-0.01	0.14
Lutein and Zeaxanthin (µg/ml)						
Baseline	790	0.21	0.08	997	0.21	0.07
AV-1	786	0.21	0.08	998	0.22	0.08
AV-1 - Baseline	785	0.00	0.06	997	0.01	0.05
Retinol (µg/ml)						
Baseline	790	0.60	0.11	997	0.60	0.12
AV-1	786	0.63	0.13	998	0.61	0.12
AV-1 - Baseline	785	0.03	0.09	997	0.01	0.08

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

Table 2.9 (Continued)
Blood Specimen Analysis: HRT Participants

Data as of: February 29, 2000

	Without Uterus			With Uterus		
	N	Mean*	S.D.*	N	Mean*	S.D.*
Clotting Factor						
Factor VII Activity, Antigen (%)						
Baseline	769	126.66	23.44	967	122.77	22.64
AV-1	758	137.96	29.62	974	129.76	25.63
AV-1 – Baseline	738	11.38	21.94	949	6.74	18.48
Factor VII C (%)						
Baseline	751	128.57	22.37	949	124.76	21.55
AV-1	745	136.42	27.30	964	125.70	23.60
AV-1 – Baseline	710	7.49	20.95	923	0.42	17.89
Fibrinogen (mg/dl)						
Baseline	769	311.34	50.30	965	307.24	49.28
AV-1	755	304.39	46.92	971	298.49	47.62
AV-1 – Baseline	735	-8.82	43.37	944	-8.81	47.77
Hormones / Other						
Glucose (mg/dl)						
Baseline	787	103.84	25.12	994	102.26	22.19
AV-1	784	101.91	23.95	996	100.07	19.26
AV-1 – Baseline	780	-2.22	15.20	992	-2.21	14.84
Insulin (μIU/ml)						
Baseline	774	12.52	5.82	982	11.67	5.23
AV-1	779	11.65	5.48	977	11.66	6.13
AV-1 – Baseline	763	-0.98	4.08	966	-0.01	4.82

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

Table 2.9 (Continued)
Blood Specimen Analysis: HRT Participants

Data as of: February 29, 2000

	Without Uterus			With Uterus		
	N	Mean*	S.D.*	N	Mean*	S.D.*
Lipoproteins						
HDL-2 (mg/dl)						
Baseline	777	17.38	6.61	974	17.56	6.49
AV-1	773	19.81	7.73	984	19.02	6.96
AV-1 – Baseline	761	2.31	4.27	962	1.42	3.80
HDL-3 (mg/dl)						
Baseline	778	39.63	6.90	974	39.20	6.72
AV-1	775	41.97	7.76	985	40.38	6.39
AV-1 – Baseline	763	2.10	4.77	963	1.22	4.34
HDL-C (mg/dl)						
Baseline	785	57.13	12.16	995	56.78	11.98
AV-1	783	61.68	14.11	997	59.40	12.05
AV-1 – Baseline	779	4.43	7.72	994	2.63	6.72
LDL-C (mg/dl)						
Baseline	774	140.42	28.60	985	139.63	27.38
AV-1	771	125.68	27.00	982	127.82	26.91
AV-1 – Baseline	762	-14.75	22.95	975	-11.80	22.36
Lp(a) (mg/dl)						
Baseline	776	26.19	21.63	982	26.47	22.19
AV-1	774	25.42	22.47	988	24.29	21.75
AV-1 – Baseline	764	-0.94	8.99	975	-2.05	9.41
Total Cholesterol (mg/dl)						
Baseline	789	228.59	31.11	997	226.01	30.93
AV-1	785	221.17	31.10	997	216.89	29.67
AV-1 – Baseline	783	-7.55	24.86	996	-9.15	24.41
Triglyceride (mg/dl)						
Baseline	789	159.95	95.63	997	147.38	60.99
AV-1	785	173.86	135.58	996	148.23	57.35
AV-1 – Baseline	783	14.49	70.39	995	0.81	43.58

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

Table 2.10
Bone Mineral Density Analysis: HRT Participants

Data as of: February 29, 2000

	Without Uterus			With Uterus		
	N	Mean	S.D.	N	Mean	S.D.
Whole Body Scan						
Baseline[1]	937	1.01	0.11	1025	0.99	0.10
AV-1	839	1.01	0.11	929	1.00	0.10
AV-3	577	1.03	0.11	609	1.02	0.10
AV-1 % Change from baseline BMD[2]	837	0.43	2.78	927	0.27	2.35
AV-3 % Change from baseline BMD[3]	575	1.67	3.61	607	1.71	3.60
Spine Scan						
Baseline	910	0.97	0.16	1002	0.95	0.16
AV-1	818	0.99	0.16	905	0.97	0.16
AV-3	569	1.00	0.17	600	0.99	0.17
AV-1 % Change from baseline BMD	816	1.90	4.57	902	2.08	4.36
AV-3 % Change from baseline BMD	566	3.40	6.31	598	4.01	5.93
Hip Scan						
Baseline	933	0.86	0.14	1024	0.84	0.13
AV-1	837	0.86	0.14	928	0.84	0.13
AV-3	577	0.88	0.15	612	0.86	0.14
AV-1 % Change from baseline BMD	834	0.71	3.27	927	0.62	3.15
AV-3 % Change from baseline BMD	574	2.18	4.70	611	2.07	4.72

[1] Measured in (g/cm^2).

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

[3] AV3 % Change from baseline BMD is defined as ((AV3-Baseline)/Baseline)x100

Table 2.11
Lost-to-Follow-up and Vital Status by Hysterectomy Status

Data as of: February 29, 2000

	With Uterus (N=16609)		Without Uterus (N=10739)		HRT Participants (N=27348)	
	N	%	N	%	N	%
Vital Status/Participation						
Deceased	192	1.2	163	1.5	355	1.3
Alive: Current Participation[1]	15768	94.9	9971	92.8	25739	94.1
Alive: Recent Participation[2]	248	1.5	232	2.2	480	1.8
Alive: Past/Unknown Participation[3]	8	0.0	9	0.1	17	0.1
Stopped Follow-Up[4]	184	1.1	148	1.4	332	1.2
Lost to Follow-Up[5]	209	1.3	216	2.0	425	1.6

[1] Participants who have filled in a Form 33 within the last 9 months.
[2] Participants who last filled in a Form 33 between 9 and 18 months ago.
[3] Participiants without a Form 33 within the last 18 months, who have been located (as indicated on Form 23) within the last 6 months.
[4] Participants with codes 5 (no follow-up) or 8 (absolutely no follow-up) on Form 7.
[5] Participants not in any of the above categories.

Table 2.12
Locally Verified Outcomes (Annualized Percentages) by Ethnicity for Hormone Replacement Therapy

Data as of: February 29, 2000

Outcomes	Total		Minority[1]		White	
Number randomized	27348		5318		22030	
Mean follow-up (months)	37.0		36.0		37.3	
Cardiovascular						
CHD[2]	306	(0.36%)	45	(0.28%)	261	(0.38%)
Coronary death	85	(0.10%)	19	(0.12%)	66	(0.10%)
Total MI[3]	240	(0.28%)	31	(0.19%)	209	(0.31%)
Clinical MI	235	(0.28%)	30	(0.19%)	205	(0.30%)
Definite Silent MI	10	(0.01%)	2	(0.01%)	8	(0.01%)
Possible Silent MI	35	(0.04%)	8	(0.05%)	27	(0.04%)
Angina	410	(0.49%)	68	(0.43%)	342	(0.50%)
CABG/PTCA	353	(0.42%)	46	(0.29%)	307	(0.45%)
Carotid artery disease	88	(0.10%)	6	(0.04%)	82	(0.12%)
Congestive heart failure	190	(0.23%)	34	(0.21%)	156	(0.23%)
Stroke	203	(0.24%)	40	(0.25%)	163	(0.24%)
PVD	56	(0.07%)	9	(0.06%)	47	(0.07%)
DVT	128	(0.15%)	14	(0.09%)	114	(0.17%)
PE	76	(0.09%)	9	(0.06%)	67	(0.10%)
CHD[2]/Possible Silent MI	336	(0.40%)	52	(0.33%)	284	(0.41%)
Coronary disease[4]	846	(1.00%)	140	(0.88%)	706	(1.03%)
DVT/PE	173	(0.20%)	19	(0.12%)	154	(0.22%)
Total CVD	1261	(1.49%)	201	(1.26%)	1060	(1.55%)
Cancer						
Breast cancer[5]	270	(0.32%)	29	(0.18%)	241	(0.35%)
Invasive breast cancer	209	(0.25%)	24	(0.15%)	185	(0.27%)
In situ breast cancer	62	(0.07%)	5	(0.03%)	57	(0.08%)
Ovary cancer	26	(0.03%)	2	(0.01%)	24	(0.04%)
Endometrial Cancer[6]	21	(0.04%)	2	(0.03%)	19	(0.04%)
Colorectal cancer	104	(0.12%)	21	(0.13%)	83	(0.12%)
Other cancer[7,8]	358	(0.42%)	45	(0.28%)	313	(0.46%)
Total cancer	771	(0.91%)	98	(0.61%)	673	(0.98%)
Fractures						
Hip fracture	74	(0.09%)	3	(0.02%)	71	(0.10%)
Vertebral fracture	78	(0.09%)	1	(0.01%)	77	(0.11%)
Other fracture[7,9]	1221	(1.45%)	138	(0.87%)	1083	(1.58%)
Total fracture	1343	(1.59%)	140	(0.88%)	1203	(1.76%)
Deaths						
Cardiovascular deaths	110	(0.13%)	22	(0.14%)	88	(0.13%)
Cancer deaths	131	(0.16%)	17	(0.11%)	114	(0.17%)
Deaths: other known cause	40	(0.05%)	4	(0.03%)	36	(0.05%)
Deaths: unknown cause	13	(0.02%)	3	(0.02%)	10	(0.01%)
Deaths: not yet adjudicated	61	(0.07%)	16	(0.10%)	45	(0.07%)
Total death	355	(0.42%)	62	(0.39%)	293	(0.43%)

[1] Participants with unmarked ethnicity are classified as Minority.

[2] "CHD" includes clinical MI, definite silent MI, and coronary death.

[3] "Total MI" includes clinical MI and definite silent MI.

[4] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

[5] Excludes three case with borderline malignancy.

[6] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

[7] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[8] Excludes non-melanoma skin cancer

[9] "Other fracture" excludes fractures indicated as pathological.

Table 2.12 (Continued)
Locally Verified Outcomes (Annualized Percentages) by Age for Hormone Replacement Therapy

Data as of: February 29, 2000

Outcome	50-54		55-59		60-69		70-79	
Number randomized	3426		5407		12362		6153	
Mean follow-up (months)	42.6		39.0		36.0		34.5	
Cardiovascular								
CHD[1]	22	(0.18%)	25	(0.14%)	149	(0.40%)	110	(0.62%)
Coronary death	5	(0.04%)	7	(0.04%)	42	(0.11%)	31	(0.18%)
Total MI[2]	18	(0.15%)	18	(0.10%)	117	(0.32%)	87	(0.49%)
Clinical MI	17	(0.14%)	18	(0.10%)	114	(0.31%)	86	(0.49%)
Definite Silent MI	2	(0.02%)	1	(0.01%)	5	(0.01%)	2	(0.01%)
Possible Silent MI	5	(0.04%)	5	(0.03%)	12	(0.03%)	13	(0.07%)
Angina	15	(0.12%)	54	(0.31%)	203	(0.55%)	138	(0.78%)
CABG/PTCA	16	(0.13%)	43	(0.24%)	173	(0.47%)	121	(0.68%)
Carotid artery disease	1	(0.01%)	11	(0.06%)	42	(0.11%)	34	(0.19%)
Congestive heart failure	9	(0.07%)	20	(0.11%)	78	(0.21%)	83	(0.47%)
Stroke	7	(0.06%)	19	(0.11%)	98	(0.26%)	79	(0.45%)
PVD	3	(0.02%)	4	(0.02%)	28	(0.08%)	21	(0.12%)
DVT	9	(0.07%)	14	(0.08%)	63	(0.17%)	42	(0.24%)
PE	4	(0.03%)	9	(0.05%)	33	(0.09%)	30	(0.17%)
CHD[1]/Possible Silent MI	27	(0.22%)	28	(0.16%)	159	(0.43%)	122	(0.69%)
Coronary disease[3]	45	(0.37%)	90	(0.51%)	399	(1.08%)	312	(1.77%)
DVT/PE	10	(0.08%)	20	(0.11%)	84	(0.23%)	59	(0.33%)
Total CVD	65	(0.54%)	131	(0.75%)	606	(1.64%)	459	(2.60%)
Cancer								
Breast cancer[4]	33	(0.27%)	38	(0.22%)	138	(0.37%)	61	(0.35%)
Invasive breast cancer	25	(0.21%)	33	(0.19%)	105	(0.28%)	46	(0.26%)
In situ breast cancer	8	(0.07%)	5	(0.03%)	35	(0.09%)	14	(0.08%)
Ovary cancer	0	(0.00%)	4	(0.02%)	16	(0.04%)	6	(0.03%)
Endometrial Cancer[5]	0	(0.00%)	2	(0.02%)	10	(0.04%)	9	(0.09%)
Colorectal cancer	7	(0.06%)	10	(0.06%)	50	(0.14%)	37	(0.21%)
Other cancer[6,7]	29	(0.24%)	43	(0.24%)	167	(0.45%)	119	(0.67%)
Total cancer	69	(0.57%)	96	(0.55%)	376	(1.02%)	230	(1.30%)
Fractures								
Hip fracture	3	(0.02%)	3	(0.02%)	19	(0.05%)	49	(0.28%)
Vertebral fracture	3	(0.02%)	9	(0.05%)	33	(0.09%)	33	(0.19%)
Other fracture[6,8]	147	(1.21%)	189	(1.07%)	581	(1.57%)	304	(1.72%)
Total fracture	151	(1.24%)	197	(1.12%)	625	(1.69%)	370	(2.09%)
Deaths								
Cardiovascular deaths	5	(0.04%)	8	(0.05%)	49	(0.13%)	48	(0.27%)
Cancer deaths	5	(0.04%)	12	(0.07%)	60	(0.16%)	54	(0.31%)
Deaths: other known cause	4	(0.03%)	6	(0.03%)	18	(0.05%)	12	(0.07%)
Deaths: unknown cause	1	(0.01%)	2	(0.01%)	5	(0.01%)	5	(0.03%)
Deaths: not yet adjudicated	6	(0.05%)	3	(0.02%)	26	(0.07%)	26	(0.15%)
Total death	21	(0.17%)	31	(0.18%)	158	(0.43%)	145	(0.82%)

[1] "CHD" includes clinical MI, definite silent MI, and coronary death.

[2] "Total MI" includes clinical MI and definite silent MI.

[3] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

[4] Excludes three case with borderline malignancy.

[5] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

[6] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[7] Excludes non-melanoma skin cancer

[8] "Other fracture" excludes fractures indicated as pathological.

Table 2.13
Locally Verified Outcomes (Annualized Percentages) for HRT Participants Without and With Uterus

Data as of: February 29, 2000

Outcomes	Without Uterus		With Uterus	
Number randomized	10739		16609	
Mean follow-up (months)	37.1		37.0	
Cardiovascular				
CHD[1]	135	(0.41%)	171	(0.33%)
Coronary death	40	(0.12%)	45	(0.09%)
Total MI[2]	104	(0.31%)	136	(0.27%)
Clinical MI	101	(0.30%)	134	(0.26%)
Definite Silent MI	6	(0.02%)	4	(0.01%)
Possible Silent MI	14	(0.04%)	21	(0.04%)
Angina	227	(0.68%)	183	(0.36%)
CABG/PTCA	182	(0.55%)	171	(0.33%)
Carotid artery disease	46	(0.14%)	42	(0.08%)
Congestive heart failure	115	(0.35%)	75	(0.15%)
Stroke	104	(0.31%)	99	(0.19%)
PVD	27	(0.08%)	29	(0.06%)
DVT	35	(0.11%)	93	(0.18%)
PE	20	(0.06%)	56	(0.11%)
CHD[1]/Possible Silent MI	146	(0.44%)	190	(0.37%)
Coronary disease[3]	439	(1.32%)	407	(0.79%)
DVT/PE	47	(0.14%)	126	(0.25%)
Total CVD	614	(1.85%)	647	(1.26%)
Cancer				
Breast cancer[4]	95	(0.29%)	175	(0.34%)
Invasive breast cancer	67	(0.20%)	142	(0.28%)
In situ breast cancer	28	(0.08%)	34	(0.07%)
Ovary cancer	6	(0.02%)	20	(0.04%)
Endometrial Cancer	0	(0.00%)	21	(0.04%)
Colorectal cancer	56	(0.17%)	48	(0.09%)
Other cancer[5,6]	133	(0.40%)	225	(0.44%)
Total cancer	289	(0.87%)	482	(0.94%)
Fractures				
Hip fracture	25	(0.08%)	49	(0.10%)
Vertebral fracture	29	(0.09%)	49	(0.10%)
Other fracture[5,7]	488	(1.47%)	733	(1.43%)
Total fracture	529	(1.59%)	814	(1.59%)
Deaths				
Cardiovascular deaths	52	(0.16%)	58	(0.11%)
Cancer deaths	58	(0.17%)	73	(0.14%)
Deaths: other known cause	13	(0.04%)	27	(0.05%)
Deaths: unknown cause	11	(0.03%)	2	(0.00%)
Deaths: not yet adjudicated	29	(0.09%)	32	(0.06%)
Total death	163	(0.49%)	192	(0.38%)

[1] "CHD" includes clinical MI, definite silent MI, and coronary death.

[2] "Total MI" includes clinical MI and definite silent MI.

[3] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

[4] Excludes three case with borderline malignancy.

[5] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[6] Excludes non-melanoma skin cancer

[7] "Other fracture" excludes fractures indicated as pathological.

Table 2.14
Counts (Annualized Percentages) of Participants with Self-Reported Outcomes by Ethnicity and Age for Hormone Replacement Therapy

Data as of: February 29, 2000

Outcomes	Total		Ethnicity: Minority[1]		Ethnicity: White	
Number randomized	27348		5318		22030	
Mean follow-up (months)	37.0		36.0		37.3	
Hospitalizations						
Ever	6568	(7.78%)	1122	(7.04%)	5446	(7.96%)
Two or more	2412	(2.86%)	404	(2.53%)	2008	(2.93%)
Other						
Diabetes (treated)	1929	(2.29%)	713	(4.47%)	1216	(1.78%)
Gallbladder disease[2]	1058	(1.25%)	190	(1.19%)	868	(1.27%)
Hysterectomy[3]	274	(0.54%)	29	(0.37%)	245	(0.57%)
Glaucoma	1298	(1.54%)	353	(2.21%)	945	(1.38%)
Osteoporosis	2375	(2.81%)	339	(2.13%)	2036	(2.97%)
Osteoarthritis[4]	3895	(4.96%)	851	(5.68%)	3044	(4.79%)
Rheumatoid arthritis	893	(1.06%)	346	(2.17%)	547	(0.80%)
Intestinal polyps	1547	(1.83%)	266	(1.67%)	1281	(1.87%)
Lupus	146	(0.17%)	31	(0.19%)	115	(0.17%)
Kidney Stones[4]	304	(0.52%)	73	(0.67%)	231	(0.49%)
Cataracts[4]	4156	(7.15%)	739	(6.78%)	3417	(7.24%)
Pills for hypertension	8020	(9.50%)	2094	(13.13%)	5926	(8.66%)

Outcome	Age: 50-54		Age: 55-59		Age: 60-69		Age: 70-79	
Number randomized	3426		5407		12362		6153	
Mean follow-up (months)	42.6		39.0		35.95		34.45	
Hospitalizations								
Ever	610	(5.02%)	1043	(5.93%)	3043	(8.22%)	1872	(10.60%)
Two or more	204	(1.68%)	351	(2.00%)	1134	(3.06%)	723	(4.09%)
Other								
Diabetes (treated)	229	(1.89%)	398	(2.26%)	890	(2.40%)	412	(2.33%)
Gallbladder disease[2]	139	(1.14%)	220	(1.25%)	489	(1.32%)	210	(1.19%)
Hysterectomy[3]	24	(0.33%)	46	(0.40%)	135	(0.60%)	69	(0.68%)
Glaucoma	103	(0.85%)	186	(1.06%)	610	(1.65%)	399	(2.26%)
Osteoporosis	132	(1.09%)	327	(1.86%)	1109	(2.99%)	807	(4.57%)
Osteoarthritis[4]	336	(3.02%)	630	(3.87%)	1771	(5.14%)	1158	(6.92%)
Rheumatoid arthritis	112	(0.92%)	190	(1.08%)	387	(1.04%)	204	(1.15%)
Intestinal polyps	136	(1.12%)	230	(1.31%)	789	(2.13%)	392	(2.22%)
Lupus	24	(0.20%)	26	(0.15%)	69	(0.19%)	27	(0.15%)
Kidney Stones[4]	36	(0.47%)	55	(0.47%)	148	(0.57%)	65	(0.52%)
Cataracts[4]	135	(1.76%)	430	(3.66%)	2077	(7.95%)	1514	(12.04%)
Pills for hypertension	756	(6.22%)	1371	(7.80%)	3657	(9.87%)	2236	(12.66%)

[1] Participants with unmarked ethnicity are classified as Minority.

[2] "Gallbladder disease" includes self-reports of both hospitalized and non-hospitalized events.

[3] Only women without a baseline hysterectomy are used to compute the annual rates of hysterectomy.

[4] These outcomes have not been self-reported on all versions of Form 33. The annualized percentages are corrected for the different amounts of follow-up.

Table 2.15
Sensitivity of HRT Study Power to Adherence and Incidence Rate Assumptions

Outcome	Year	Intervention Effect[1] (%)	Percentage of Cases[1]				Power				
			Intervention		Control		ERT vs. Placebo		PERT vs. Placebo		Combined HRT vs. Placebo
			Design	Revised[2]	Design	Revised[2]	Design[3]	Revised Adherence & Incidence Rates[4]	Design[3]	Revised Adherence & Incidence Rates[4]	
CHD	2001	17	2.71	2.01	3.26	2.41	46	32	54	41	63
		21	2.60	1.93	3.26	2.40	62	44	70	56	79
		24	2.49	1.84	3.25	2.39	76	57	84	70	91
	2004	17	4.16	3.50	5.03	4.15	64	47	73	59	82
		21	3.97	3.35	5.02	4.13	81	63	88	76	94
		24	3.79	3.20	5.01	4.11	92	77	96	88	99

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

[2] Revised incidence rates reflect greater healthy volunteer effects (67%, 50%, 37%) in years 1-3.

[3] Combined Drop-out and loss to follow-up rates of 7.9% in year 1, 4.9% per year thereafter; Drop-in rate of 1.5% per year.

[4] Combined Drop-out and loss to follow-up rates of 9.8% in year 1, 8.4% in year 2, and 6.9% per year thereafter; Drop-in rate of 2.5% per year. Average follow-up is 8.5 years.

3. DM Component

3.1 Recruitment

Age-specific DM recruitment data are presented in *Table 3.1*. The age distributions exceeded the design assumptions for ages 50-54, 55-59, and 60-69. For the age category 70-79, recruitment was lower than designed.

3.2 Adherence

Nutrient intake data for adherence monitoring are presented in *Tables 3.2-3.4 and Figure 3.1*. Studywide, the mean difference between Intervention and Control women is 11.0% energy from fat at AV-1, 10.1% at AV-2, 9.7% at AV-3, 8.9% at AV-4, and 8.5% at AV-5. These results are based on only those women providing a food frequency questionnaire at the designated visit. Missing data account for 11.5% of our sample at AV-1 and 15.2% at AV-3. The C-I value in minority women is roughly 1-2 percentage points below the full sample. (*Table 3.4*). The trend in the C-I is concerning, although the AV3 – AV5 estimates are likely somewhat reduced by the early cohort effect. That is, women randomized early in WHI received higher fat gram goals than the majority of WHI participants, who were randomized after implementation of reduced fat gram goals. At AV-4, the C-I difference is almost 1 percentage point larger for women who have reduced fat gram goals than the original goals. Overall, 81% of DM Intervention participants have reduced fat gram goals. Acknowledging the early cohort effect, the overall C-I for percent energy from fat is roughly 2 to 3 percentage points lower than the original design assumptions. Refer to Sections 3.7 and 3.8 for a discussion of the impact of the C-I on study power and the advanced adherence initiatives that are underway. For fruit and vegetable intake, the mean difference between the arms of the trial is in excess of 1 more serving per day for Intervention vs. Control women and holding steady. The mean difference between the two arms of the trial for grain servings is nearly 1 more serving per day of grains for Intervention vs. Control women.

Multivariate analyses were conducted to identify factors associated with C-I differences in percentage energy from fat (*Tables 3.5-3.6*). Participant characteristics associated with a lower C-I difference include being older and a minority. Body weight data are presented in *Table 3.7*. On average, the difference in body weight between Control and Intervention participants at AV-1 was 2 kg, with a return to 0.1 kg by AV-5. Participants with revised fat gram goals have maintained a C-I difference of 1.0 kg. From a trend perspective, these results are consistent with changes in energy intake estimated with the FFQ. Several DM participation variables, including attending sessions, making up missed sessions and self-monitoring, have significant positive impacts on the C-I difference at AV-1 and AV-2 (*Table 3.6*). Missing sessions (i.e., Eligible for Make-up Maintenance Sessions) is associated with a large negative C-I and self-monitoring has a substantial positive impact at all AVs.

3.3 Blood Specimen and Bone Density Analyses

Table 3.8 presents the results of blood specimens analyses from a small (4.3%) cohort of DM women selected randomly at baseline for these prospective analyses. This subsample incorporated oversampling of minorities. The results shown here are weighted to reflect the overall WHI distribution of race/ethnicity. Differences between baseline and AV-1 are mostly modest, with

reductions of about 5% in LDL cholesterol and about 3% in total cholesterol on average for Intervention and Control women combined. There are no substantial changes in HDL-cholesterol or triglycerides in the combined groups. Note that baseline and AV-1 specimens were batched together for concurrent analyses by Medical Research Labs.

Table 3.9 presents blinded bone mineral density data from the DM bone density subsample. Again, changes from baseline to AV-1 or AV-3 are interesting with increases in mean bone mineral density in the whole body scan as well as the spine and hip scan. An increase in BMD was not expected from this intervention. Possible reasons for this observation include use of calcium supplements and/or HRT, selection of healthy conscious women, incomplete BMD data (14% at AV-3) or measurement issues. This topic warrants further investigation.

3.4 Adherence to Follow-up

Table 3.10 summarizes adherence to follow-up contacts by treatment arm and contact type. Follow-up participation has been roughly equivalent in the two arms. The acceptable adherence rates specified by the Steering Committee for collection of outcome data are 90% at AV-1, with a decline of no more than 1% per year. WHI follow-up contact adherence rates are above or at these rates for Years 1 through 5 with no substantial difference by arm.

3.5 Vital Status

Table 3.11 presents data on the vital status and the participation status of participants in the DM trial. A detailed description of CCC and clinic activities to actively locate participants who do not complete their periodic visits is given in *Section 5 – Outcomes*. For operational purposes, we define CT participants to have an "unknown" participation status if there is no outcomes information from the participant for 18 months, and no other contacts for 6 months. Currently about 2.9% of the DM participants are lost-to-follow-up or have stopped follow-up, and 1.1% of the participants are known to be deceased. Virtually all of the remaining participants have completed a *Form 33 – Medical History Update* in the last 18 months. The design assumed that 3% per year would be lost to follow-up or death. Currently the average follow-up for DM participants is about 3.2 years, suggesting that approximately 9.3% could be expected to be dead or lost to follow-up. Our overall rates compare favorably to design assumptions.

3.6 Outcomes

Table 3.12 contains counts of the number of locally verified major WHI outcomes for DM participants by ethnicity and age. Approximately 10-15% of the self-reported outcomes have not yet been verified, so the numbers in this table can be seen as a lower bound to the actual number of outcomes that have occurred. Compared to the design assumptions, we have observed almost 90% of the expected number of breast cancers, 75% of the expected number of colorectal cancers, about 65% of the expected number of CHD events, and about 30% of the expected number hip fractures.

Table 3.13 contains counts of the number of self-reports for some outcomes that are not locally verified in WHI. As most of the locally verified outcomes are somewhat over-reported (see *Section 6.3 – Outcomes Data Quality)* the number in this table should be taken as an upper bound to the number of events that have occurred in DM participants.

3.7 Power Considerations

While the observed Comparison - Intervention (C-I) differences represent a substantial achievement, they fall short of the assumptions of 13% C-I at AV-1 and subsequent decline of 0.25% per year. The lower than anticipated value of C-I at AV-1 will reduce the overall power of the study but the size of the impact depends considerably on the degree of adherence throughout the remaining years of follow-up. The power calculations shown in *Table 3.14* were calculated under two patterns of adherence assumptions. The first set is based on existing C-I values of 11% at AV-1, and 10% at AV-2 with a projected decline to 8% by year 10. The second scenario again starts at 11% but stays at 10% throughout the remaining follow-up. Using the final sample size and age distribution of DM participants and 8.5 years of follow-up on average, the study has about 63% power for breast cancer and 79% power for colorectal cancer under the first adherence assumptions. We could obtain 73% power for breast cancer and 80% for colorectal cancer, if the C-I values were 11% at AV-1 and 10% at all subsequent time points. These calculations suggest that this second adherence pattern is the level of performance we must aim to achieve. We note that the intervention effect modeling for design considerations was based on percent of energy from fat. Other changes associated with the low fat eating pattern (e.g., increases in fruits, vegetables, and grains) would likely improve the power as these changes may have additional, complementary prevention effects.

3.8 Issues

As noted above, the C-I difference is less than that specified in the design assumptions. The WHI investigators and staff have undertaken a number of activities addressing adherence. Most notably, in summer 1999 the DM Intervention began implementation of an Intensive Intervention Program incorporating motivational interviewing techniques and modeled after the pilot study that was completed in 1998. Nutritionists and other staff conducting this intensive intervention participated in a two-day training on motivational interviewing techniques. Nutritionists are prioritizing their efforts by working first with "medium adherers," defined as women who are attending some sessions but not meeting their fat gram goal or not self-monitoring. Medium adherers comprise slightly less than 40% of all DM Intervention participants. As of March 31, 2000, 39% of medium adherers had received at least one motivational interviewing contact. The study goal is to complete a series of three motivational interviewing contacts with all medium adherers by December 2000. When Clinical Center resources permit, nutritionists are also contacting high and low-adherers.

WHI investigators and staff continue to incorporate additional adherence initiatives for incorporation into the WHI DM Intervention. During the Fall 1999 Annual WHI meeting, the Steering Committee and Project Office approved the concept of a tailored message campaign using multiple modalities of written materials and follow-up telephone calls. Consultants responsible for developing the Polyp Prevention Trial Campaigns have been retained to help develop this new intervention initiative for WHI. This campaign will include all DM Intervention participants, is being introduced later this year, and mailings will begin in early 2001.

Table 3.1
Dietary Modification Component Age - Specific Recruitment

Data as of: February 29, 2000

	Total Randomized	% of Overall Goal	Age Distribution	Design Assumption
DM	**48,837**			
50-54	6958	149%	14%	10
55-59	11042	118%	23%	20
60-69	22714	108%	47%	45
70-79	8123	70%	17%	25

Table 3.2
Nutrient Intake Monitoring
Data as of: February 29, 2000

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
% Energy from Fat									
FFQ Baseline	19542	38.8	5.0	29295	38.8	5.0	0.0	0.0	0.82
FFQ Year 1[3]	18075	25.1	7.5	26729	36.1	6.9	11.0	0.1	0.00
FFQ Year 2[4]	5378	26.1	7.6	7937	36.2	7.0	10.1	0.1	0.00
FFQ Year 3[5]	1206	26.9	7.7	1715	36.6	6.9	9.7	0.3	0.00
FFQ Year 4[6]	533	28.2	7.9	872	37.1	7.0	8.9	0.4	0.00
FFQ Year 5[7]	210	28.2	7.5	327	36.7	7.0	8.5	0.6	0.00
4DFR Baseline	892	32.8	6.4	1351	33.0	6.8	0.2	0.3	0.54
4DFR Year 1	804	21.7	7.3	1171	32.9	6.8	11.2	0.3	0.00
24 Hr Recall, Post-baseline	226	23.0	9.2	262	32.1	7.6	9.1	0.8	0.00
24 Hr Recall, Year 1	210	22.5	8.0	261	32.5	7.8	10.0	0.7	0.00
24 Hr Recall, Year 2	153	23.1	9.5	180	32.2	8.3	9.1	1.0	0.00
24 Hr Recall, Year 3	75	25.0	8.7	107	33.9	8.4	8.9	1.3	0.00
24 Hr Recall, Year 3 Cohort	410	24.4	8.4	638	32.8	7.2	8.4	0.5	0.00
24 Hr Recall, Year 4	41	26.3	8.2	54	32.0	7.5	5.7	1.6	0.00
Total Energy (kcal)									
FFQ Baseline	19542	1789	713	29295	1789	707	0	6.6	0.94
FFQ Year 1	18075	1474	534	26729	1584	641	110	5.8	0.00
FFQ Year 2	5378	1484	535	7937	1576	624	92	10.4	0.00
FFQ Year 3	1206	1495	539	1715	1586	658	91	23.0	0.00
FFQ Year 4	533	1483	543	872	1575	650	92	33.6	0.04
FFQ Year 5	210	1489	528	327	1563	625	74	52.1	0.40
4DFR Baseline	892	1707	454	1351	1713	459	6	19.7	0.79
4DFR Year 1	804	1423	356	1171	1627	447	204	18.9	0.00
24 Hr Recall, Post-baseline	226	1520	418	262	1653	516	133	43.0	0.00
24 Hr Recall, Year 1	210	1496	420	261	1631	487	135	42.5	0.00
24 Hr Recall, Year 2	153	1472	432	180	1623	545	151	54.6	0.04
24 Hr Recall, Year 3	75	1505	392	107	1734	563	229	75.3	0.01
24 Hr Recall, Year 3 Cohort	410	1472	396	638	1637	484	165	28.6	0.00
24 Hr Recall, Year 4	41	1537	394	54	1547	465	10	90.3	0.77
Total Fat (g)									
FFQ Baseline	19542	77.9	35.3	29295	77.8	34.7	0.1	0.3	0.87
FFQ Year 1	18075	41.5	21.8	26729	64.5	31.7	23.0	0.3	0.00
FFQ Year 2	5378	43.2	22.1	7937	64.3	31.3	21.1	0.5	0.00
FFQ Year 3	1206	45.2	23.6	1715	65.5	32.5	20.3	1.1	0.00
FFQ Year 4	533	46.9	24.2	872	65.5	32.0	18.6	1.6	0.00
FFQ Year 5	210	47.4	24.4	327	65.1	32.6	17.7	2.6	0.00
4DFR Baseline	892	63.0	23.6	1351	63.8	24.6	0.8	1.0	0.71
4DFR Year 1	804	34.1	14.5	1171	60.4	23.5	26.3	0.9	0.00
24 Hr Recall, Post-baseline	226	39.6	21.9	262	60.5	26.9	20.9	2.2	0.00
24 Hr Recall, Year 1	210	37.4	17.5	261	60.4	25.5	23.0	2.1	0.00
24 Hr Recall, Year 2	153	38.1	21.2	180	59.8	28.8	21.7	2.8	0.00
24 Hr Recall, Year 3	75	41.8	18.3	107	67.2	31.6	25.4	4.1	0.00
24 Hr Recall, Year 3 Cohort	410	40.5	19.4	638	61.2	25.3	20.7	1.5	0.00
24 Hr Recall, Year 4	41	44.5	17.0	54	56.6	24.3	12.1	4.4	0.01

(continues)

[1] Absolute difference.

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

[3] 4947 (27%) Intervention women had <=20% energy from fat at year 1.

[4] 1193 (22%) Intervention women had <=20% energy from fat at year 2.

[5] 234 (23%) Intervention women had <=20% energy from fat at year 3

[6] 72 (14%) Intervention women had <=20% energy from fat at year 4.

[7] 34 (16%) Intervention women had <=20% energy from fat at year 5.

Table 3.2 (continued)
Nutrient Intake Monitoring

Data as of: February 29, 2000

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
Saturated Fat (g)									
FFQ Baseline	19542	27.4	13.4	29295	27.3	13.2	0.1	0.1	0.85
FFQ Year 1[3]	18075	14.2	8.1	26729	22.5	11.9	8.3	0.1	0.00
FFQ Year 2[4]	5378	14.7	8.2	7937	22.4	11.7	7.7	0.2	0.00
FFQ Year 3[5]	1206	15.4	8.7	1715	22.9	12.3	7.5	0.4	0.00
FFQ Year 4[6]	533	16.2	8.9	872	22.9	11.7	6.7	0.6	0.00
FFQ Year 5[7]	210	16.2	8.6	327	22.7	11.8	6.5	0.9	0.00
4DFR Baseline	892	20.6	8.9	1351	20.9	9.3	0.3	0.4	0.72
4DFR Year 1	804	10.6	5.2	1171	19.5	8.3	8.9	0.3	0.00
24 Hr Recall, Post-baseline	226	12.9	7.9	262	20.1	9.6	7.2	0.8	0.00
24 Hr Recall, Year 1	210	11.9	6.4	261	20.1	10.5	8.2	0.8	0.00
24 Hr Recall, Year 2	153	12.1	7.3	180	19.5	10.4	7.4	1.0	0.00
24 Hr Recall, Year 3	75	14.1	7.2	107	23.1	12.3	9.0	1.6	0.00
24 Hr Recall, Year 3 Cohort	410	12.7	7.2	638	20.1	9.0	7.4	0.5	0.00
24 Hr Recall, Year 4	41	14.7	6.5	54	18.9	9.7	4.2	1.8	0.02
Polyunsaturated Fat (g)									
FFQ Baseline	19542	15.3	7.6	29295	15.3	7.6	0.0	0.1	0.78
FFQ Year 1	18075	7.9	4.4	26729	12.5	6.7	4.6	0.1	0.00
FFQ Year 2	5378	8.2	4.5	7937	12.4	6.5	4.2	0.1	0.00
FFQ Year 3	1206	8.7	4.9	1715	12.6	6.5	3.9	0.2	0.00
FFQ Year 4	533	9.0	5.0	872	12.7	6.9	3.7	0.3	0.00
FFQ Year 5	210	9.1	5.0	327	12.6	7.2	3.5	0.6	0.00
4DFR Baseline	892	13.1	5.8	1351	13.5	6.1	0.4	0.3	0.40
4DFR Year 1	804	7.4	3.4	1171	12.7	6.2	5.3	0.2	0.00
24 Hr Recall, Post-baseline	226	8.3	5.0	262	12.6	7.3	4.3	0.6	0.00
24 Hr Recall, Year 1	210	7.9	4.5	261	12.3	6.3	4.4	0.5	0.00
24 Hr Recall, Year 2	153	8.1	5.6	180	12.6	7.9	4.5	0.8	0.00
24 Hr Recall, Year 3	75	8.4	5.1	107	13.6	7.4	5.2	1.0	0.00
24 Hr Recall, Year 3 Cohort	410	8.8	4.7	638	12.7	6.5	3.9	0.4	0.00
24 Hr Recall, Year 4	41	9.1	4.1	54	10.9	5.7	1.8	1.1	0.07
Fruits and Vegetables (servings)									
FFQ Baseline	19471	3.6	1.8	29217	3.6	1.8	0.0	0.0	0.69
FFQ Year 1	17994	5.0	2.3	26647	3.8	2.0	1.2	0.0	0.00
FFQ Year 2	5414	5.1	2.4	7994	3.9	2.0	1.2	0.0	0.00
FFQ Year 3	1260	5.1	2.4	1821	3.9	2.0	1.2	0.1	0.00
FFQ Year 4	552	5.1	2.4	889	3.9	2.0	1.2	0.1	0.00
FFQ Year 5	221	5.2	2.5	347	3.9	2.2	1.3	0.2	0.00
Grain Servings (Not including desserts/pastries)									
FFQ Baseline	19469	4.7	2.5	29215	4.8	2.5	0.1	0.0	0.43
FFQ Year 1	17990	5.1	2.7	26637	4.2	2.3	0.9	0.0	0.00
FFQ Year 2	5413	4.9	2.5	7988	4.1	2.2	0.8	0.0	0.00
FFQ Year 3	1260	4.9	2.6	1820	4.1	2.3	0.8	0.1	0.00
FFQ Year 4	552	4.7	2.5	887	4.1	2.4	0.6	0.1	0.00
FFQ Year 5	221	4.6	2.3	347	3.9	2.2	0.7	0.2	0.00

[1] Absolute difference.

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

[3] 4947 (27%) Intervention women had <=20% energy from fat at year 1.

[4] 1193 (22%) Intervention women had <=20% energy from fat at year 2.

[5] 234 (23%) Intervention women had <=20% energy from fat at year 3

[6] 72 (14%) Intervention women had <=20% energy from fat at year 4.

[7] 34 (16%) Intervention women had <=20% energy from fat at year 5.

Figure 3.1
Nutrient Intake: Intervention vs. Control

Data as of: February 29, 2000

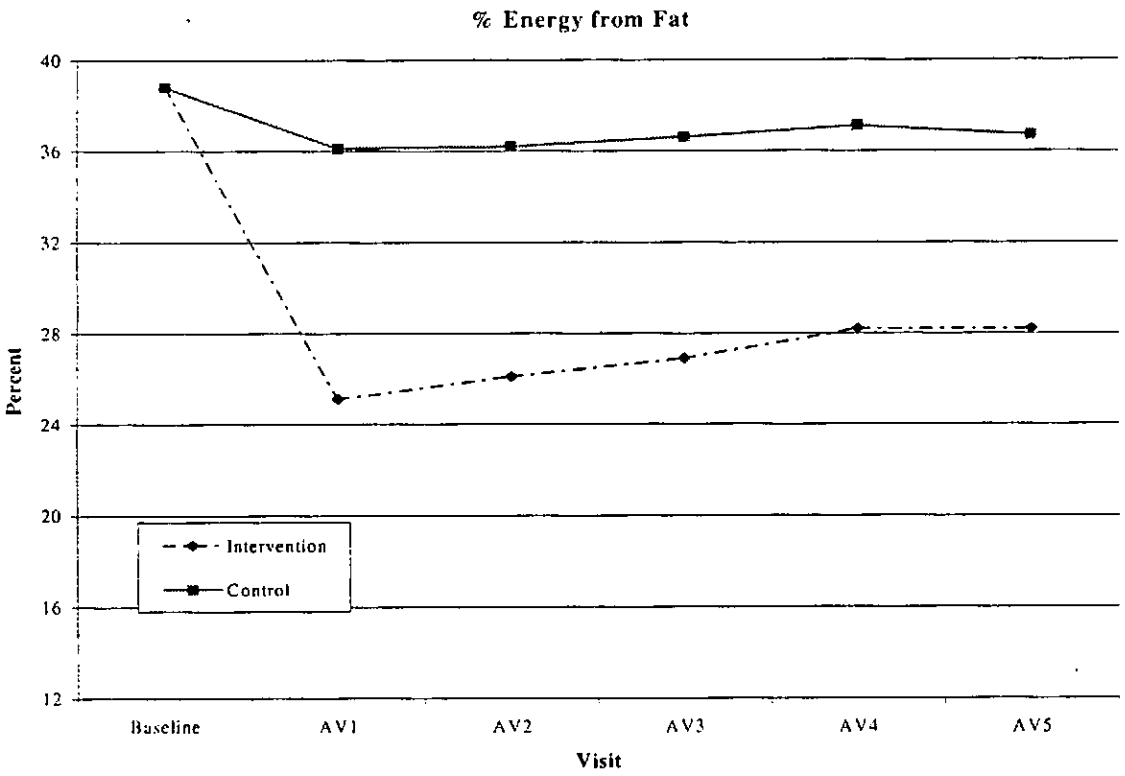
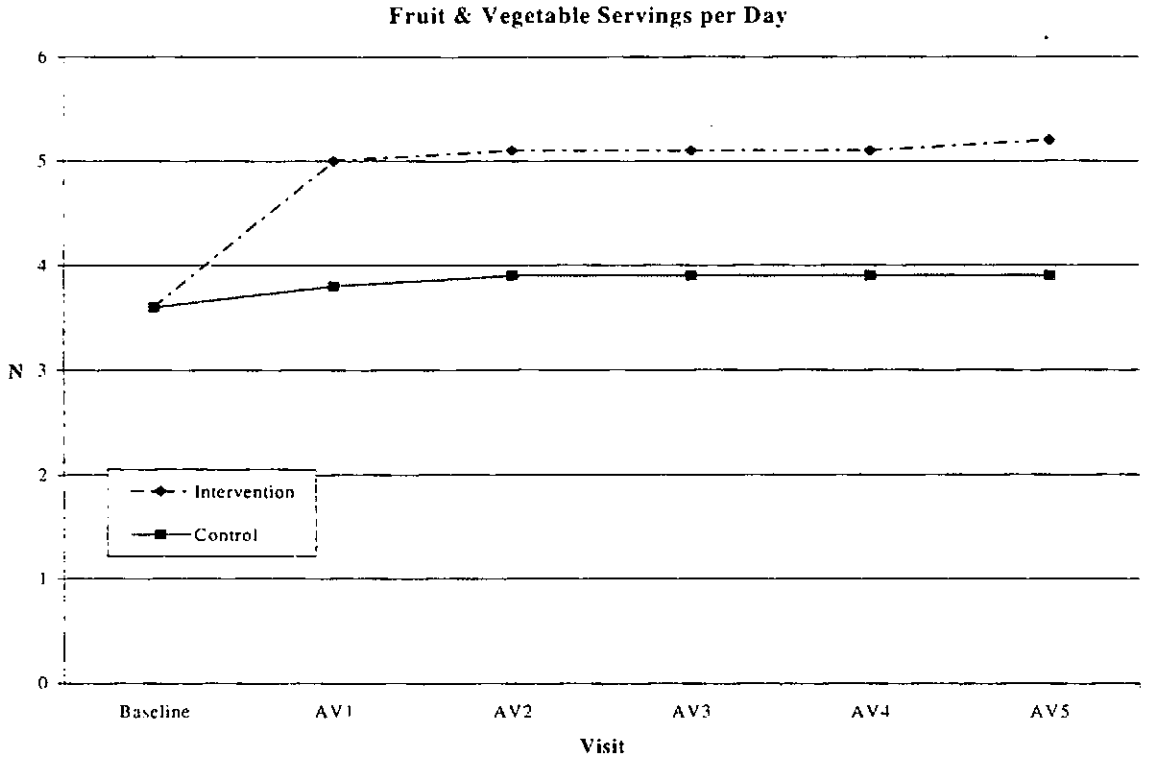


Figure 3.1 (continued)
Nutrient Intake: Intervention vs. Control

Data as of: February 29, 2000



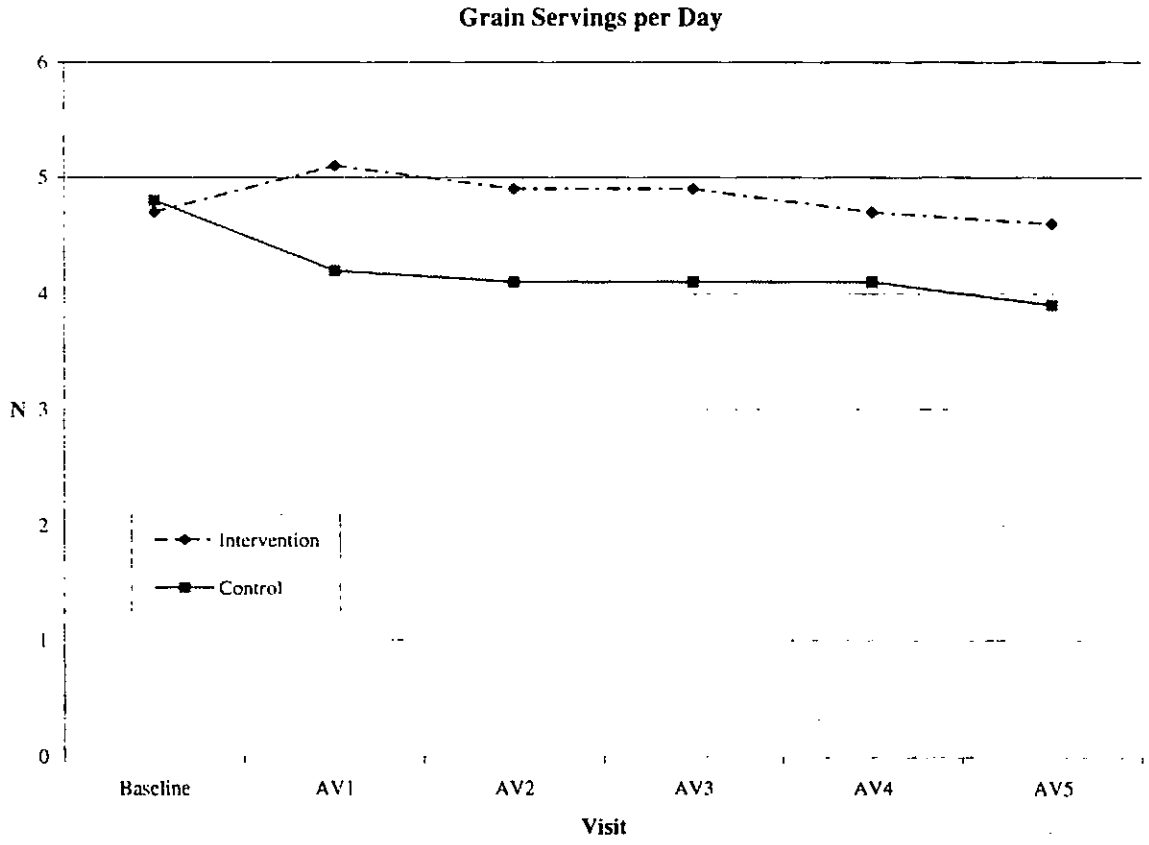


Table 3.3
Nutrient Intake Monitoring For Women With Revised Fat Gram Goals

Data as of: February 29, 2000

	Intervention[1]			Control[2]			Difference		
	N	Mean	SD	N	Mean	SD	Mean[3]	SE	p-value[4]
% Energy from Fat									
FFQ Baseline	15858	38.8	5.0	23754	38.8	4.9	0.0	0.1	0.48
FFQ Year 1	14646	25.3	7.6	21724	36.2	6.9	10.9	0.1	0.00
FFQ Year 2	4326	26.3	7.7	6279	36.5	7.0	10.2	0.1	0.00
FFQ Year 3	798	27.3	8.0	1192	37.2	6.7	9.9	0.3	0.00
FFQ Year 4	210	28.2	8.5	398	38.0	6.7	9.8	0.6	0.00
4DFR Baseline	691	32.4	6.5	1038	33.0	6.9	0.6	0.3	0.06
4DFR Year 1	621	21.6	7.5	892	33.1	6.9	11.5	0.4	0.00
24 Hr Recall, Post-baseline	186	23.4	9.4	205	32.1	7.7	8.7	0.9	0.00
24 Hr Recall, Year 1	161	22.3	8.0	193	32.6	7.8	10.3	0.8	0.00
24 Hr Recall, Year 2	116	22.4	8.8	119	31.9	8.3	9.5	1.1	0.00
24 Hr Recall, Year 3	29	23.8	9.0	51	32.9	8.3	9.1	2.0	0.00
24 Hr Recall, Year 3 Cohort	244	24.3	8.4	388	33.2	7.4	8.9	0.6	0.00
Total Energy (kcal)									
FFQ Baseline	15858	1780	701	23754	1786	706	6	7.2	0.47
FFQ Year 1	14646	1468	533	21724	1588	644	120	6.4	0.00
FFQ Year 2	4326	1475	537	6279	1578	627	103	11.7	0.00
FFQ Year 3	798	1480	523	1192	1601	672	121	28.2	0.00
FFQ Year 4	210	1439	567	398	1617	695	178	55.8	0.00
4DFR Baseline	691	1688	455	1038	1713	469	25	22.8	0.30
4DFR Year 1	621	1405	362	892	1621	447	216	21.6	0.00
24 Hr Recall, Post-baseline	186	1499	418	205	1640	524	141	48.3	0.00
24 Hr Recall, Year 1	161	1495	428	193	1648	502	153	50.1	0.00
24 Hr Recall, Year 2	116	1468	429	119	1600	519	132	62.2	0.17
24 Hr Recall, Year 3	29	1607	390	51	1731	619	124	127.4	0.50
24 Hr Recall, Year 3 Cohort	244	1471	393	388	1617	483	146	36.8	0.00
Total Fat (g)									
FFQ Baseline	15858	77.4	34.6	23754	77.6	34.6	0.2	0.4	0.63
FFQ Year 1	14646	41.6	22.0	21724	64.9	31.9	23.3	0.3	0.00
FFQ Year 2	4326	43.2	22.6	6279	64.9	31.5	21.7	0.6	0.00
FFQ Year 3	798	45.4	23.2	1192	67.1	33.3	21.7	1.4	0.00
FFQ Year 4	210	45.4	24.9	398	68.8	34.3	23.4	2.7	0.00
4DFR Baseline	691	61.5	23.3	1038	63.8	25.1	2.3	1.2	0.12
4DFR Year 1	621	33.6	14.9	892	60.5	23.9	26.9	1.1	0.00
24 Hr Recall, Post-baseline	186	39.7	22.1	205	60.2	27.7	20.5	2.6	0.00
24 Hr Recall, Year 1	161	36.7	16.7	193	61.2	25.9	24.5	2.4	0.00
24 Hr Recall, Year 2	116	37.0	20.2	119	58.5	28.1	21.5	3.2	0.00
24 Hr Recall, Year 3	29	42.7	19.3	51	65.4	33.3	22.7	6.8	0.00
24 Hr Recall, Year 3 Cohort	244	40.2	19.5	388	61.4	25.6	21.2	1.9	0.00

(continues)

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

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

[3] Absolute difference.

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

Table 3.3 (continued)
Nutrient Intake Monitoring For Women With Revised Fat Gram Goals

Data as of: February 29, 2000

	Intervention[1]			Control[2]			Difference		
	N	Mean	SD	N	Mean	SD	Mean[3]	SE	p-value[4]
Saturated Fat (g)									
FFQ Baseline	15858	27.2	13.2	23754	27.2	13.1	0.0	0.1	0.82
FFQ Year 1	14646	14.2	8.1	21724	22.6	11.9	8.4	0.1	0.00
FFQ Year 2	4326	14.7	8.4	6279	22.6	11.8	7.9	0.2	0.00
FFQ Year 3	798	15.4	8.6	1192	23.3	12.6	7.9	0.5	0.00
FFQ Year 4	210	15.6	9.0	398	24.0	12.5	8.4	1.0	0.00
4DFR Baseline	691	20.0	8.8	1038	20.8	9.5	0.8	0.5	0.16
4DFR Year 1	621	10.3	5.3	892	19.3	8.3	9.0	0.4	0.00
24 Hr Recall, Post-baseline	186	13.0	8.0	205	20.0	9.7	7.0	0.9	0.00
24 Hr Recall, Year 1	161	11.5	6.1	193	20.4	10.8	8.9	1.0	0.00
24 Hr Recall, Year 2	116	11.6	7.0	119	18.9	9.6	7.3	1.1	0.00
24 Hr Recall, Year 3	29	15.1	7.9	51	22.9	14.2	7.8	2.9	0.00
24 Hr Recall, Year 3 Cohort	244	12.4	7.5	388	20.0	8.9	7.6	0.7	0.00
Polyunsaturated Fat (g)									
FFQ Baseline	15858	15.1	7.4	23754	15.1	7.4	0.0	0.1	0.54
FFQ Year 1	14646	7.9	4.4	21724	12.5	6.7	4.6	0.1	0.00
FFQ Year 2	4326	8.3	4.5	6279	12.5	6.6	4.2	0.1	0.00
FFQ Year 3	798	8.7	4.8	1192	13.0	6.7	4.3	0.3	0.00
FFQ Year 4	210	8.7	5.0	398	13.4	7.2	4.7	0.6	0.00
4DFR Baseline	691	12.8	5.7	1038	13.5	6.3	0.7	0.3	0.06
4DFR Year 1	621	7.4	3.5	892	12.9	6.5	5.5	0.3	0.00
24 Hr Recall, Post-baseline	186	8.3	5.1	205	12.4	7.4	4.1	0.6	0.00
24 Hr Recall, Year 1	161	7.8	4.4	193	12.4	6.1	4.6	0.6	0.00
24 Hr Recall, Year 2	116	8.1	5.0	119	12.3	7.7	4.2	0.8	0.00
24 Hr Recall, Year 3	29	8.1	5.3	51	12.9	7.3	4.8	1.5	0.00
24 Hr Recall, Year 3 Cohort	244	8.9	4.6	388	12.7	6.5	3.8	0.5	0.00
Fruits and Vegetables (servings)									
FFQ Baseline	15817	3.6	1.8	23708	3.6	1.8	0.0	0.0	0.64
FFQ Year 1	14597	5.0	2.3	21668	3.9	2.0	1.1	0.0	0.00
FFQ Year 2	4370	5.1	2.4	6350	3.9	2.0	1.2	0.0	0.00
FFQ Year 3	856	5.1	2.4	1305	3.9	2.1	1.2	0.1	0.00
FFQ Year 4	232	5.1	2.5	421	3.8	2.0	1.3	0.2	0.00
Grain Servings (Not including desserts/pastries)									
FFQ Baseline	15815	4.7	2.5	23706	4.8	2.5	0.1	0.0	0.21
FFQ Year 1	14593	5.0	2.6	21659	4.2	2.3	0.8	0.0	0.00
FFQ Year 2	4369	4.9	2.5	6345	4.1	2.2	0.8	0.0	0.00
FFQ Year 3	856	4.7	2.5	1304	4.1	2.3	0.6	0.1	0.00
FFQ Year 4	232	4.4	2.3	421	4.2	2.7	0.2	0.2	0.13

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

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

[3] Absolute difference.

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

Table 3.4
Nutrient Intake Monitoring in Minority Women

Data as of: February 29, 2000

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
% Energy from Fat									
FFQ Baseline	3626	39.4	5.2	5352	39.4	5.2	0.0	0.1	0.50
FFQ Year 1[3]	3151	27.7	8.2	4555	36.5	7.3	8.8	0.2	0.00
FFQ Year 2[4]	960	28.5	8.0	1333	36.4	7.2	7.9	0.3	0.00
FFQ Year 3[5]	215	29.1	8.4	307	37.0	6.9	7.9	0.7	0.00
FFQ Year 4[6]	75	29.7	7.7	116	36.9	7.4	7.2	1.1	0.00
FFQ Year 5	23	30.1	7.0	29	35.4	5.5	5.3	1.7	0.00
4DFR Baseline	450	33.0	6.4	683	33.3	6.9	0.3	0.4	0.46
4DFR Year 1	400	22.9	7.7	562	33.4	7.0	10.5	0.5	0.00
24 Hr Recall, Post-baseline	40	24.6	10.7	43	30.6	7.6	6.0	2.0	0.00
24 Hr Recall, Year 1	34	22.7	7.0	42	31.4	7.4	8.7	1.7	0.00
24 Hr Recall, Year 2	24	24.8	11.1	37	29.6	9.1	4.8	2.6	0.09
24 Hr Recall, Year 3	13	26.9	9.2	15	36.3	9.0	9.4	3.4	0.02
24 Hr Recall, Year 3 Cohort	175	25.1	8.1	258	33.1	7.5	8.0	0.8	0.00
Total Energy (kcal)									
FFQ Baseline	3626	1763	812	5352	1756	825	7.0	17.6	0.44
FFQ Year 1	3151	1420	636	4555	1515	767	95.0	16.6	0.00
FFQ Year 2	960	1425	683	1333	1499	737	74.0	30.3	0.08
FFQ Year 3	215	1450	631	307	1570	840	120.0	67.7	0.27
FFQ Year 4	75	1399	669	116	1546	889	147.0	120.0	0.35
FFQ Year 5	23	1222	447	29	1340	703	118.0	168.6	0.94
4DFR Baseline	450	1671	481	683	1687	470	16.0	28.8	0.46
4DFR Year 1	400	1384	375	562	1601	467	217.0	28.2	0.00
24 Hr Recall, Post-baseline	40	1470	492	43	1599	415	129.0	99.7	0.10
24 Hr Recall, Year 1	34	1477	395	42	1498	387	21.0	90.1	0.82
24 Hr Recall, Year 2	24	1483	525	37	1501	583	18.0	147.1	0.73
24 Hr Recall, Year 3	13	1299	312	15	1607	596	308.0	184.2	0.15
24 Hr Recall, Year 3 Cohort	175	1432	379	258	1545	441	113.0	40.8	0.01
Total Fat (g)									
FFQ Baseline	3626	77.9	39.9	5352	77.7	40.2	0.2	0.9	0.60
FFQ Year 1	3151	44.1	26.7	4555	62.7	37.1	18.6	0.8	0.00
FFQ Year 2	960	45.5	29.5	1333	62.1	36.5	16.6	1.4	0.00
FFQ Year 3	215	48.3	29.5	307	65.7	40.5	17.4	3.2	0.00
FFQ Year 4	75	46.3	26.6	116	63.8	39.3	17.5	5.2	0.00
FFQ Year 5	23	41.6	19.6	29	54.2	33.8	12.6	7.9	0.29
4DFR Baseline	450	61.9	23.2	683	63.6	25.7	1.7	1.5	0.44
4DFR Year 1	400	35.2	15.9	562	60.5	24.8	25.3	1.4	0.00
24 Hr Recall, Post-baseline	40	40.0	22.8	43	55.2	21.7	15.2	4.9	0.00
24 Hr Recall, Year 1	34	36.9	14.6	42	53.7	20.5	16.8	4.2	0.00
24 Hr Recall, Year 2	24	43.9	30.6	37	51.0	27.7	7.1	7.6	0.35
24 Hr Recall, Year 3	13	39.4	16.5	15	66.5	32.2	27.1	9.9	0.01
24 Hr Recall, Year 3 Cohort	175	40.3	17.7	258	58.4	24.3	18.1	2.1	0.00

(continues)

[1] Absolute difference.

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

[3] 574 (18%) Intervention women had <=20% energy from fat at year 1.

[4] 153 (16%) Intervention women had <=20% energy from fat at year 2.

[5] 29 (13%) Intervention women had <=20% energy from fat at year 3

[6] 5 (7%) Intervention women had <=20% energy from fat at year 4.

Table 3.4 (continued)
Nutrient Intake Monitoring in Minority Women

Data as of: February 29, 2000

	Intervention			Control			Difference		
	N	Mean	SD	N	Mean	SD	Mean[1]	SE	p-value[2]
Saturated Fat (g)									
FFQ Baseline	3626	26.0	14.2	5352	25.9	14.5	0.1	0.3	0.64
FFQ Year 1[3]	3151	14.5	9.3	4555	20.7	12.9	6.2	0.3	0.00
FFQ Year 2[4]	960	14.9	10.6	1333	20.6	12.8	5.7	0.5	0.00
FFQ Year 3[5]	215	15.8	10.2	307	21.7	14.8	5.9	1.2	0.00
FFQ Year 4[6]	75	15.6	9.2	116	20.6	12.8	5.0	1.7	0.00
FFQ Year 5	23	13.3	6.1	29	17.7	10.9	4.4	2.5	0.25
4DFR Baseline	450	19.5	8.5	683	20.3	9.4	0.8	0.5	0.32
4DFR Year 1	400	10.7	5.7	562	18.9	8.3	8.2	0.5	0.00
24 Hr Recall, Post-baseline	40	12.4	7.5	43	18.0	8.7	5.6	1.8	0.00
24 Hr Recall, Year 1	34	11.6	6.3	42	15.9	6.9	4.3	1.5	0.00
24 Hr Recall, Year 2	24	13.6	10.2	37	15.3	8.0	1.7	2.3	0.41
24 Hr Recall, Year 3	13	13.4	7.2	15	20.8	9.7	7.4	3.3	0.03
24 Hr Recall, Year 3 Cohort	175	12.2	5.9	258	18.4	8.3	6.2	0.7	0.00
Polyunsaturated Fat (g)									
FFQ Baseline	3626	15.9	8.6	5352	15.8	8.6	0.1	0.2	0.49
FFQ Year 1	3151	8.8	5.6	4555	12.8	7.9	4.0	0.2	0.00
FFQ Year 2	960	9.0	5.8	1333	12.5	7.7	3.5	0.3	0.00
FFQ Year 3	215	9.8	6.4	307	13.2	7.9	3.4	0.7	0.00
FFQ Year 4	75	8.9	5.6	116	13.7	9.4	4.8	1.2	0.00
FFQ Year 5	23	8.1	4.4	29	11.2	7.5	3.1	1.8	0.22
4DFR Baseline	450	13.4	6.0	683	13.7	6.5	0.3	0.4	0.59
4DFR Year 1	400	7.8	3.7	562	13.2	6.7	5.4	0.4	0.00
24 Hr Recall, Post-baseline	40	8.9	5.3	43	11.5	6.0	2.6	1.2	0.01
24 Hr Recall, Year 1	34	7.8	3.1	42	12.5	5.5	4.7	1.1	0.00
24 Hr Recall, Year 2	24	9.3	7.2	37	10.9	8.5	1.6	2.1	0.39
24 Hr Recall, Year 3	13	7.4	3.2	15	13.7	7.7	6.3	2.3	0.02
24 Hr Recall, Year 3 Cohort	175	9.0	4.9	258	12.5	6.5	3.5	0.6	0.00
Fruits and Vegetables (servings)									
FFQ Baseline	3617	3.3	1.9	5348	3.2	1.9	0.1	0.0	0.10
FFQ Year 1	3139	4.5	2.5	4549	3.4	2.0	1.1	0.1	0.00
FFQ Year 2	964	4.6	2.5	1339	3.4	2.1	1.2	0.1	0.00
FFQ Year 3	225	4.6	2.4	323	3.7	2.2	0.9	0.2	0.00
FFQ Year 4	80	4.6	2.9	118	3.8	2.5	0.8	0.4	0.01
FFQ Year 5	26	5.0	2.4	33	3.5	2.3	1.5	0.6	0.01
Grain Servings (Not including desserts/pastries)									
FFQ Baseline	3617	4.8	2.9	5347	4.7	2.9	0.1	0.1	0.51
FFQ Year 1	3138	4.8	2.9	4547	4.2	2.7	0.6	0.1	0.00
FFQ Year 2	964	4.6	2.9	1338	4.1	2.6	0.5	0.1	0.00
FFQ Year 3	225	4.6	2.8	323	4.2	2.7	0.4	0.2	0.03
FFQ Year 4	80	4.4	2.7	118	4.3	3.4	0.1	0.5	0.56
FFQ Year 5	26	3.8	1.7	33	3.4	2.5	0.4	0.6	0.10

[1] Absolute difference.

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

[3] 574 (18%) Intervention women had <=20% energy from fat at year 1.

[4] 153 (16%) Intervention women had <=20% energy from fat at year 2.

[5] 29 (13%) Intervention women had <=20% energy from fat at year 3

[6] 5 (7%) Intervention women had <=20% energy from fat at year 4.

Table 3.5
Multivariate Analysis of Study Subject Characteristics
on Control - Intervention Difference in % Energy from Fat from FFQ at AV-1:

Data as of: February 29, 2000

Study Subject Characteristics		C - I (%)[1]
		N=44415
Age	50-54 vs. 60-69	0.39
	55-59 vs. 60-69	0.35 *
	70-79 vs. 60-69	-1.29 **
Ethnicity	Black vs. White	-1.61 **
	Hispanic vs. White	-1.83 **
	Other Minority vs. White	-1.24 **
Education	0-8 Years vs. Post H.S.	0.27
	Some H.S. or Diploma vs. Post H.S.	0.05
Marital Status	Not Married vs. Married	-0.09
Family Income	<20K vs. ≥75K	-0.70 **
	20-35K vs. ≥75K	-0.23
	35-50K vs. ≥75K	0.06
	50-75K vs. ≥75K	-0.04
HRT Randomized	Yes vs. No	0.49 **
BMI - Mean(BMI)	BMI - 29.12	-0.03 *
Hysterectomy	Yes vs. No	-0.02

[1] Model adjusted for clinic effects.
* Indicates p-value <.05 from two-sided t-test.
** Indicates p-value <.01 from two-sided t-test.

Table 3.5 (continued)
Multivariate Analysis of Study Subject Characteristics
on Control - Intervention Difference in % Energy from Fat from FFQ at AV-2:

Data as of: February 29, 2000

Study Subject Characteristics		C - I (%)[1]
		N=13320
Age	50-54 vs. 60-69	-0.30
	55-59 vs. 60-69	0.10
	70-79 vs. 60-69	-1.52 **
Ethnicity	Black vs. White	-2.47 **
	Hispanic vs. White	-0.32
	Other Minority vs. White	-1.07
Education	0-8 Years vs. Post H.S.	-0.99
	Some H.S. or Diploma vs. Post H.S.	-0.14
Marital Status	Not Married vs. Married	-0.62 *
Family Income	<20K vs. >75K	0.02
	20-35K vs. >75K	0.56
	35-50K vs. >75K	0.47
	50-75K vs. >75K	0.24
HRT Randomized	Yes vs. No	0.51
BMI - Mean(BMI)	BMI - 29.12	-0.07 **
Hysterectomy	Yes vs. No	-0.52 *

[1] Model adjusted for clinic effects.
* Indicates p-value <.05 from two-sided t-test.
** Indicates p-value <.01 from two-sided t-test.

Table 3.5 (continued)
Multivariate Analysis of Study Subject Characteristics
on Control - Intervention Difference in % Energy from Fat from FFQ at AV-3:

Data as of: February 29, 2000

Study Subject Characteristics		C - I (%)[1]
		N=3017
Age	50-54 vs. 60-69	0.15
	55-59 vs. 60-69	0.61
	70-79 vs. 60-69	0.12
Ethnicity	Black vs. White	0.25
	Hispanic vs. White	-1.04
	Other Minority vs. White	-1.81
Education	0-8 Years vs. Post H.S.	0.11
	Some H.S. or Diploma vs. Post H.S.	-0.83
Marital Status	Not Married vs. Married	0.44
Family Income	<20K vs. ≥75K	-0.55
	20-35K vs. ≥75K	-0.30
	35-50K vs. ≥75K	-0.19
	50-75K vs. ≥75K	-0.33
HRT Randomized	Yes vs. No	-0.43
BMI - Mean(BMI)	BMI - 29.12	-0.04
Hysterectomy	Yes vs. No	0.09

[1] Model adjusted for clinic effects.
* Indicates p-value <.05 from two-sided t-test.
** Indicates p-value <.01 from two-sided t-test.

Table 3.6
Effects of DM Intervention Participation Variables
on Control - Intervention Difference in % Energy from Fat from FFQ at AV-1:

Data as of: February 29, 2000

DM Implementation/Participation	C-I % Energy from Fat[1] N=44804	C-I % Energy from Fat[1] N=44804
Intervention Group Size	-0.002	-0.01
Days from Randomization to Intervention Group/100	-0.57 **	-0.43 **
% Assigned Sessions Attended by AV-1 (10% change)	1.08 **	0.41 **
Eligible for ≥1 Make-up Session by AV-1	-2.35 **	-1.45 **
% Sessions Made-up by AV-1 (10% change)	0.37 **	0.16 **
Fat Gram Goal	0.05 **	0.03 *
% Assigned Sessions (out of 3-18) Providing Fat Scores by AV-1 (10% change)		0.34 **

[1] Model adjusted for clinic effects and terms with listed coefficients.

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

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

Table 3.6 (continued)
Effects of DM Intervention Participation Variables
on Control - Intervention Difference in % Energy from Fat from FFQ at AV-2:

Data as of: February 29. 2000

DM Implementation/Participation	C-I % Energy from Fat[1] N=13425	C-I % Energy from Fat[1] N=13425
Intervention Group Size	0.01	0.01
Days from Randomization to Intervention Group/100	0.34 **	0.36 **
% Assigned Sessions Attended by AV-2 (10% change)	0.79 **	0.46 **
Eligible for ≥1 Make-up Session by AV-2	-1.89 **	-0.96
% Sessions Made-up by AV-2 (10% change)	0.34 **	0.19 **
% Assigned Maintenance Sessions Attended by AV-2 (10% change)	0.28 **	0.09 *
Eligible for ≥ Make-up Maintenance Session by AV-2	-0.82 *	-0.68 *
% Assigned Maintenance Sessions Made-up by AV-2 (10% change)	0.16 **	0.06
Fat Gram Goal	0.006	0.0001
% Assigned Sessions (out of 3-18) Providing Fat Scores by AV-2 (10% change)		0.41 **
% Assigned Maintenance Sessions Providing Fat Scores by AV-2 (10% change)		0.24 **

[1] Model adjusted for clinic effects and terms with listed coefficients.

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

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

Table 3.6 (continued)
Effects of DM Intervention Participation Variables
on Control - Intervention Difference in % Energy from Fat from FFQ at AV-3:

Data as of: February 29, 2000

DM Implementation/Participation	C-I % Energy from Fat[1] N=3040	C-I % Energy from Fat[1] N=3040
Intervention Group Size	0.003	
Days from Randomization to Intervention Group/100	0.16	
% Assigned Sessions Attended by AV-3 (10% change)	0.09	
Eligible for ≥1 Make-up Session by AV-3	-0.78	
% Sessions Made-up by AV-3 (10% change)	0.05	
% Assigned Maintenance Sessions Attended by AV-2 (10% change)	-0.05	
Eligible for ≥1 Make-up Maintenance Session by AV-2	-0.43	
% Assigned Maintenance Sessions Made-up by AV-2 (10% change)	-0.10	
% Assigned Maintenance Sessions Attended by AV-3 (10% change)	-0.06	-0.03
Eligible for ≥ Make-up Maintenance Session by AV-3	-2.21 **	-2.38 **
% Assigned Maintenance Sessions Made-up by AV-3 (10% change)	0.14 *	0.15 *
Fat Gram Goal	0.09	0.08
% Assigned Sessions (out of 3-18) Providing Fat Scores by AV-2 (10% change)	-0.05	
% Assigned Maintenance Sessions Providing Fat Scores by AV-2 (10% change)	0.15	
% Assigned Sessions (out of 3-18) Providing Fat Scores by AV-3 (10% change)	0.77 **	0.85 **
% Assigned Maintenance Sessions Providing Fat Scores by AV-3 (10% change)	0.36 **	0.38 **

[1] Model adjusted for clinic effects and terms with listed coefficients.

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

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

Table 3.7
Body Weight

Data as of: February 29, 2000

Body Weight (kg)[1]	Intervention N	Intervention Mean	Intervention S.D.	Control N	Control Mean	Control S.D.	Difference Mean[2]	Difference S.E.	Difference p-value
All Participants									
Baseline	19524	76.8	16.7	29272	76.7	16.5	-0.1	0.2	0.36
Year 1	18112	74.4	16.8	26647	76.3	16.8	1.9	0.2	0.00
Year 2	15412	75.4	17.3	23095	76.6	16.9	1.2	0.2	0.00
Year 3	10794	75.6	17.2	16386	76.5	16.7	0.9	0.2	0.00
Year 4	5388	75.8	16.8	8233	76.4	16.4	0.6	0.3	0.06
Year 5	2129	75.6	16.1	3243	75.7	16.3	0.1	0.5	0.81
Minority Participants									
Baseline	3622	80.0	18.7	5351	79.4	18.9	-0.6	0.4	0.12
Year 1	3208	78.8	19.7	4617	78.9	19.2	0.1	0.4	0.90
Year 2	2646	79.3	19.4	3925	79.2	19.2	-0.1	0.5	0.88
Year 3	1768	79.7	20.2	2701	79.9	19.2	0.2	0.6	0.73
Year 4	785	80.6	18.5	1183	80.2	18.4	-0.4	0.8	0.66
Year 5	242	80.6	16.8	343	79.6	18.3	-1.0	1.5	0.50
Participants Aged 70-79									
Baseline	3247	73.0	14.7	4871	72.9	14.5	-0.1	0.3	0.81
Year 1	3005	70.7	15.2	4481	72.7	15.4	2.0	0.4	0.00
Year 2	2488	71.0	15.2	3741	72.4	15.2	1.4	0.4	0.00
Year 3	1566	70.6	15.5	2408	71.6	14.8	1.0	0.5	0.05
Year 4	704	70.3	14.2	1061	71.0	14.2	0.7	0.7	0.31
Year 5	264	70.2	15.0	439	70.9	14.6	0.7	1.1	0.58
Participants with Revised Fat Gram Goals[3]									
Baseline	15844	77.0	17.0	23739	77.0	16.9	0.0	0.2	0.79
Year 1	14656	74.6	17.1	21581	76.6	17.1	2.0	0.2	0.00
Year 2	12151	75.6	17.5	18252	76.9	17.1	1.3	0.2	0.00
Year 3	7596	75.7	17.6	11554	76.8	16.9	1.1	0.3	0.00
Year 4	2323	75.9	16.8	3538	76.9	16.7	1.0	0.4	0.04

[1] Shown for 30 <= weight (kg) <= 220

[2] Control - Intervention

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

Table 3.8
Blood Specimen Analysis: DM Participants

Data as of: February 29. 2000

	N	Mean*	S.D.*
Micronutrients			
Alpha-Carotene (µg/ml)			
Baseline	1999	0.08	0.07
AV-1	2001	0.09	0.06
AV-1 – Baseline	1997	0.00	0.05
Alpha-tocopherol (µg/ml)			
Baseline	1999	16.15	5.60
AV-1	2001	16.69	5.62
AV-1 – Baseline	1997	0.52	4.12
Beta-Carotene (µg/ml)			
Baseline	1999	0.30	0.22
AV-1	2001	0.30	0.22
AV-1 – Baseline	1997	0.00	0.18
Beta-Cryptoxanthine (µg/ml)			
Baseline	1999	0.08	0.05
AV-1	2000	0.09	0.05
AV-1 – Baseline	1996	0.00	0.04
Gamma-tocopherol (µg/ml)			
Baseline	1999	2.20	1.17
AV-1	2000	1.86	1.06
AV-1 – Baseline	1996	-0.35	0.78
Lycopene (µg/ml)			
Baseline	1999	0.42	0.16
AV-1	2001	0.41	0.16
AV-1 – Baseline	1997	-0.01	0.14
Lutein and Zeaxanthin (µg/ml)			
Baseline	1999	0.22	0.09
AV-1	2001	0.22	0.08
AV-1 – Baseline	1997	0.00	0.06
Retinol (µg/ml)			
Baseline	1999	0.61	0.12
AV-1	2001	0.61	0.12
AV-1 – Baseline	1997	0.00	0.08

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

Table 3.8 (Continued)
Blood Specimen Analysis: DM Participants

Data as of: February 29, 2000

	N	Mean*	S.D.*
Clotting Factors			
Factor VII Activity, Antigen (%)			
Baseline	1951	129.42	26.75
AV-1	1944	129.57	26.99
AV-1 - Baseline	1903	0.11	18.73
Factor VII C (%)			
Baseline	1910	129.73	26.05
AV-1	1916	127.24	25.44
AV-1 - Baseline	1844	-2.98	19.24
Fibrinogen (mg/dl)			
Baseline	1948	300.31	48.56
AV-1	1942	298.50	45.91
AV-1 - Baseline	1899	-1.82	41.28
Hormones/Other			
Glucose (mg/dl)			
Baseline	1999	100.07	21.15
AV-1	1995	98.69	20.12
AV-1 - Baseline	1991	-1.36	15.76
Insulin (µIU/ml)			
Baseline	1965	11.29	5.40
AV-1	1965	11.13	9.28
AV-1 - Baseline	1931	-0.14	8.04

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

Table 3.8 (Continued)
Blood Specimen Analysis: DM Participants

Data as of: February 29, 2000

	N	Mean*	S.D.*
Lipoproteins			
HDL-2 (mg/dl)			
Baseline	1964	18.79	7.07
AV-1	1975	19.02	7.10
AV-1 - Baseline	1943	0.28	4.34
HDL-3 (mg/dl)			
Baseline	1966	41.44	7.54
AV-1	1976	40.86	7.03
AV-1 - Baseline	1946	-0.56	4.69
HDL-C (mg/dl)			
Baseline	1992	60.16	13.14
AV-1	1996	59.89	12.55
AV-1 - Baseline	1987	-0.21	7.23
LDL-C (mg/dl)			
Baseline	1963	134.06	27.86
AV-1	1964	127.29	27.17
AV-1 - Baseline	1942	-6.85	19.40
Lp(a) (mg/dl)			
Baseline	1974	25.23	21.26
AV-1	1973	24.61	21.06
AV-1 - Baseline	1950	-0.58	8.16
Total Cholesterol (mg/dl)			
Baseline	1998	225.10	30.20
AV-1	1998	218.11	29.35
AV-1 - Baseline	1994	-7.08	21.82
Triglyceride (mg/dl)			
Baseline	1998	155.60	74.02
AV-1	1998	156.76	74.74
AV-1 - Baseline	1994	0.85	46.69

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

Table 3.9
Bone Mineral Density[1] Analysis: DM Participants

Data as of: February 29, 2000

	N	Mean	S.D.
Whole Body Scan			
Baseline	3622	1.03	0.11
AV1	3271	1.03	0.11
AV3	2842	1.04	0.11
AV1 % Change from baseline BMD[2]	3244	0.18	2.49
AV3 % Change from baseline BMD[3]	2820	1.36	3.61
Spine Scan			
Baseline	3547	0.99	0.17
AV1	3206	1.00	0.17
AV3	2784	1.01	0.17
AV1 % Change from baseline BMD	3182	0.71	3.85
AV3 % Change from baseline BMD	2764	2.16	5.22
Hip Scan			
Baseline	3620	0.87	0.14
AV1	3268	0.87	0.14
AV3	2835	0.88	0.14
AV1 % Change from baseline BMD	3250	-0.05	2.77
AV3 % Change from baseline BMD	2822	1.11	4.23

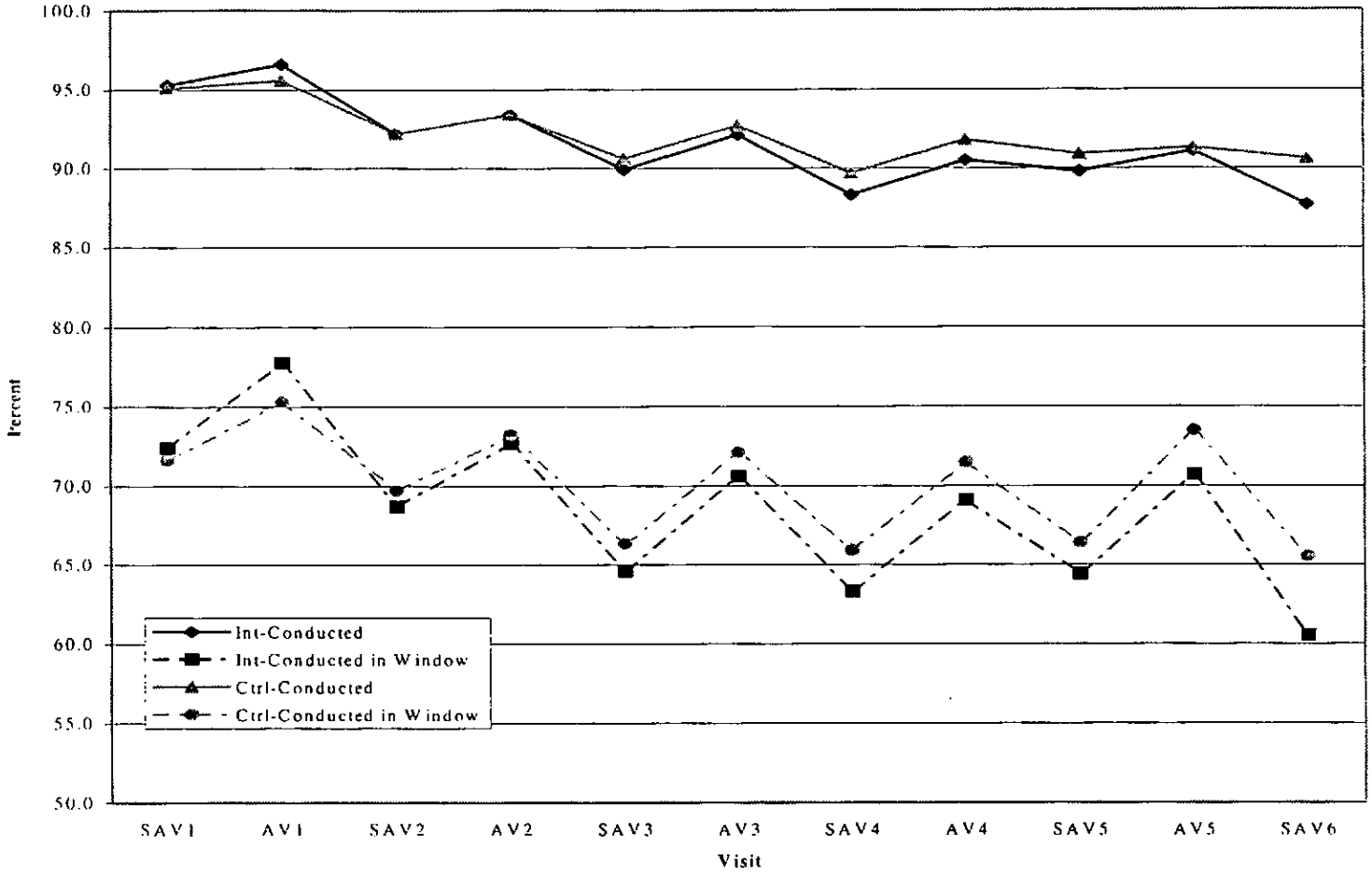
[1] Measured in (g/cm^2).

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

[3] AV3 % Change from baseline BMD is defined as ((AV3-Baseline)/Baseline)x100

Table 3.10
Adherence to Follow-up Contacts

Data as of: February 29, 2000



Contact		Due N	Conducted N	Conducted %	Conducted in window N	Conducted in window %
Semi-Annual Contact 1	Intervention	19542	18621	95.3%	14148	72.4%
	Control	29295	27855	95.1%	20983	71.6%
Annual Visit 1	Intervention	19542	18879	96.6%	15197	77.8%
	Control	29295	28002	95.6%	22051	75.3%
Semi-Annual Contact 2	Intervention	19539	18011	92.2%	13431	68.7%
	Control	29290	27008	92.2%	20406	69.7%
Annual Visit 2	Intervention	18098	16895	93.4%	13150	72.7%
	Control	27154	25364	93.4%	19866	73.2%
Semi-Annual Contact 3	Intervention	15637	14052	89.9%	10102	64.6%
	Control	23455	21242	90.6%	15554	66.3%
Annual Visit 3	Intervention	12697	11690	92.1%	8962	70.6%
	Control	19026	17640	92.7%	13721	72.1%
Semi-Annual Contact 4	Intervention	9477	8372	88.3%	6000	63.3%
	Control	14231	12760	89.7%	9381	65.9%
Annual Visit 4	Intervention	6619	5987	90.5%	4573	69.1%
	Control	9892	9078	91.8%	7071	71.5%
Semi-Annual Contact 5	Intervention	4337	3896	89.8%	2794	64.4%
	Control	6472	5880	90.9%	4296	66.4%
Annual Visit 5	Intervention	2674	2437	91.1%	1891	70.7%
	Control	3987	3639	91.3%	2932	73.5%
Semi-Annual Visit 6	Intervention	1312	1151	87.7%	794	60.5%
	Control	1983	1796	90.6%	1298	65.5%

Table 3.11
Lost-to-Follow-up and Vital Status: DM Participants

Data as of: February 29, 2000

	DM Participants (N=48837)	
	N	%
Vital Status/Participation		
Deceased	518	1.1
Alive: Current Participation[1]	45738	93.7
Alive: Recent Participation[2]	1149	2.4
Alive: Past/Unknown Participation[3]	38	0.1
Stopped Follow-Up[4]	636	1.3
Lost to Follow-Up[5]	758	1.6

[1] Participants who have filled in a Form 33 within the last 9 months.

[2] Participants who last filled in a Form 33 between 9 and 18 months ago.

[3] Participants without a Form 33 within the last 18 months, who have been located (as indicated on Form 23) within the last 6 months.

[4] Participants with codes 5 (no follow-up) or 8 (absolutely no follow-up) on Form 7.

[5] Participants not in any of the above categories.

Table 3.12
Locally Verified Outcomes (Annualized Percentages) by Ethnicity for Dietary Modification

Data as of: February 29, 2000

Outcomes	Total		Minority[1]		White	
Number randomized	48837		9076		39761	
Mean follow-up (months)	39.1		37.0		39.5	
Cancer						
Breast cancer[2]	641	(0.40%)	70	(0.25%)	571	(0.44%)
Invasive breast cancer	490	(0.31%)	53	(0.19%)	437	(0.33%)
In situ breast cancer	154	(0.10%)	17	(0.06%)	137	(0.10%)
Ovary cancer	71	(0.04%)	10	(0.04%)	61	(0.05%)
Endometrial Cancer[3]	93	(0.10%)	13	(0.09%)	80	(0.10%)
Colorectal cancer	180	(0.11%)	37	(0.13%)	143	(0.11%)
Other cancer[4,5]	638	(0.40%)	68	(0.24%)	570	(0.44%)
Total cancer	1590	(1.00%)	194	(0.69%)	1396	(1.07%)
Cardiovascular						
CHD[6]	432	(0.27%)	57	(0.20%)	375	(0.29%)
Coronary death	111	(0.07%)	15	(0.05%)	96	(0.07%)
Total MI[7]	342	(0.22%)	47	(0.17%)	295	(0.23%)
Clinical MI	331	(0.21%)	42	(0.15%)	289	(0.22%)
Definite Silent MI	17	(0.01%)	5	(0.02%)	12	(0.01%)
Possible Silent MI	59	(0.04%)	10	(0.04%)	49	(0.04%)
Angina	612	(0.38%)	109	(0.39%)	503	(0.38%)
CABG/PTCA	507	(0.32%)	60	(0.21%)	447	(0.34%)
Carotid artery disease	106	(0.07%)	14	(0.05%)	92	(0.07%)
Congestive heart failure	253	(0.16%)	48	(0.17%)	205	(0.16%)
Stroke	289	(0.18%)	52	(0.19%)	237	(0.18%)
PVD	77	(0.05%)	18	(0.06%)	59	(0.05%)
CHD[6]/Possible Silent MI	481	(0.30%)	67	(0.24%)	414	(0.32%)
Coronary disease[8]	1203	(0.76%)	199	(0.71%)	1004	(0.77%)
Total CVD	1615	(1.02%)	259	(0.93%)	1356	(1.04%)
Fractures						
Hip fracture	107	(0.07%)	7	(0.03%)	100	(0.08%)
Vertebral fracture	141	(0.09%)	9	(0.03%)	132	(0.10%)
Other fracture[4,9]	1952	(1.23%)	200	(0.72%)	1752	(1.34%)
Total fracture	2148	(1.35%)	214	(0.77%)	1934	(1.48%)
Deaths						
Cardiovascular deaths	142	(0.09%)	18	(0.06%)	124	(0.09%)
Cancer deaths	207	(0.13%)	23	(0.08%)	184	(0.14%)
Deaths: other known cause	58	(0.04%)	12	(0.04%)	46	(0.04%)
Deaths: unknown cause	20	(0.01%)	4	(0.01%)	16	(0.01%)
Deaths: not yet adjudicated	91	(0.06%)	25	(0.09%)	66	(0.05%)
Total death	518	(0.33%)	82	(0.29%)	436	(0.33%)

[1] Participants with unmarked ethnicity are classified as Minority.

[2] Excludes five cases with borderline malignancy.

[3] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

[4] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[5] Excludes non-melanoma skin cancer

[6] "CHD" includes clinical MI, definite silent MI, and coronary death.

[7] "Total MI" includes clinical MI and definite silent MI.

[8] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

[9] "Other fracture" excludes fractures indicated as pathological.

Table 3.12
Locally Verified Outcomes (Annualized Percentages) by Age for Dietary Modification

Data as of: February 29, 2000

Outcome	50-54		55-59		60-69		70-79	
Number randomized	6961		11043		22713		8120	
Mean follow-up (months)	45.3		41.3		36.9		36.7	
Cancer								
Breast cancer[1]	73	(0.28%)	156	(0.41%)	297	(0.43%)	115	(0.46%)
Invasive breast cancer	46	(0.18%)	121	(0.32%)	234	(0.33%)	89	(0.36%)
In situ breast cancer	27	(0.10%)	35	(0.09%)	65	(0.09%)	27	(0.11%)
Ovary cancer	10	(0.04%)	15	(0.04%)	30	(0.04%)	16	(0.06%)
Endometrial Cancer[2]	14	(0.09%)	23	(0.10%)	35	(0.09%)	21	(0.16%)
Colorectal cancer	9	(0.03%)	33	(0.09%)	92	(0.13%)	46	(0.19%)
Other cancer[3,4]	61	(0.23%)	103	(0.27%)	320	(0.46%)	154	(0.62%)
Total cancer	163	(0.62%)	318	(0.84%)	760	(1.09%)	349	(1.41%)
Cardiovascular								
CHD[5]	29	(0.11%)	49	(0.13%)	210	(0.30%)	144	(0.58%)
Coronary death	4	(0.02%)	8	(0.02%)	56	(0.08%)	43	(0.17%)
Total MI[6]	25	(0.10%)	43	(0.11%)	165	(0.24%)	109	(0.44%)
Clinical MI	22	(0.08%)	43	(0.11%)	158	(0.23%)	108	(0.44%)
Definite Silent MI	4	(0.02%)	1	(0.00%)	9	(0.01%)	3	(0.01%)
Possible Silent MI	6	(0.02%)	12	(0.03%)	23	(0.03%)	18	(0.07%)
Angina	42	(0.16%)	78	(0.21%)	313	(0.45%)	179	(0.72%)
CABG/PTCA	29	(0.11%)	65	(0.17%)	258	(0.37%)	155	(0.62%)
Carotid artery disease	5	(0.02%)	10	(0.03%)	49	(0.07%)	42	(0.17%)
Congestive heart failure	13	(0.05%)	25	(0.07%)	118	(0.17%)	97	(0.39%)
Stroke	14	(0.05%)	25	(0.07%)	138	(0.20%)	112	(0.45%)
PVD	2	(0.01%)	9	(0.02%)	35	(0.05%)	31	(0.12%)
CHD[5]/Possible Silent MI	35	(0.13%)	58	(0.15%)	228	(0.33%)	160	(0.64%)
Coronary disease[7]	79	(0.30%)	142	(0.37%)	598	(0.86%)	384	(1.55%)
Total CVD	96	(0.37%)	181	(0.48%)	798	(1.14%)	540	(2.18%)
Fractures								
Hip fracture	5	(0.02%)	8	(0.02%)	39	(0.06%)	55	(0.22%)
Vertebral fracture	7	(0.03%)	13	(0.03%)	64	(0.09%)	57	(0.23%)
Other fracture[3,8]	257	(0.98%)	395	(1.04%)	918	(1.31%)	382	(1.54%)
Total fracture	266	(1.01%)	413	(1.09%)	998	(1.43%)	471	(1.90%)
Deaths								
Cardiovascular deaths	4	(0.02%)	10	(0.03%)	68	(0.10%)	60	(0.24%)
Cancer deaths	14	(0.05%)	27	(0.07%)	105	(0.15%)	61	(0.25%)
Deaths: other known cause	5	(0.02%)	9	(0.02%)	24	(0.03%)	20	(0.08%)
Deaths: unknown cause	2	(0.01%)	2	(0.01%)	11	(0.02%)	5	(0.02%)
Deaths: not yet adjudicated	8	(0.03%)	5	(0.01%)	47	(0.07%)	31	(0.12%)
Total death	33	(0.13%)	53	(0.14%)	255	(0.37%)	177	(0.71%)

[1] Excludes five cases with borderline malignancy.

[2] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

[3] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[4] Excludes non-melanoma skin cancer

[5] "CHD" includes clinical MI, definite silent MI, and coronary death.

[6] "Total MI" includes clinical MI and definite silent MI.

[7] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

[8] "Other fracture" excludes fractures indicated as pathological.

Table 3.13
Counts (Annualized Percentages) of Participants with Self-Reported Outcomes by Ethnicity and Age for Dietary Modification

Data as of: February 29, 2000

Outcomes	Total		Ethnicity: Minority[1]		White	
Number randomized	48837		9076		39761	
Mean follow-up (months)	39.1		37.0		39.5	
Hospitalizations						
Ever	11852	(7.46%)	1941	(6.95%)	9911	(7.56%)
Two or more	4310	(2.71%)	664	(2.38%)	3646	(2.78%)
Other						
DVT[2]	244	(0.15%)	32	(0.11%)	212	(0.16%)
PE	112	(0.07%)	12	(0.04%)	100	(0.08%)
Diabetes (treated)	2861	(1.80%)	1033	(3.70%)	1828	(1.40%)
Gallbladder disease[3]	1919	(1.21%)	316	(1.13%)	1603	(1.22%)
Hysterectomy[4]	756	(0.84%)	103	(0.75%)	653	(0.85%)
Glaucoma	2272	(1.43%)	553	(1.98%)	1719	(1.31%)
Osteoporosis	4622	(2.91%)	610	(2.18%)	4012	(3.06%)
Osteoarthritis[5]	7585	(2.72%)	1551	(3.21%)	6034	(2.61%)
Rheumatoid arthritis	1551	(0.98%)	506	(1.81%)	1045	(0.80%)
Intestinal polyps	3098	(1.95%)	555	(1.99%)	2543	(1.94%)
Lupus	257	(0.16%)	54	(0.19%)	203	(0.15%)
Kidney Stones[5]	564	(0.53%)	112	(0.59%)	452	(0.51%)
Cataracts[5]	7099	(6.62%)	1284	(6.78%)	5815	(6.58%)
Pills for hypertension	14871	(9.35%)	3708	(13.27%)	11163	(8.52%)

Outcome	Age: 50-54		55-59		60-69		70-79	
Number randomized	6961		11043		22713		8120	
Mean follow-up (months)	45.3		41.3		36.9		36.7	
Hospitalizations								
Ever	1338	(5.09%)	2234	(5.88%)	5641	(8.07%)	2639	(10.63%)
Two or more	436	(1.66%)	747	(1.96%)	2009	(2.88%)	1118	(4.50%)
Other								
DVT[2]	21	(0.08%)	41	(0.11%)	113	(0.16%)	69	(0.28%)
PE	8	(0.03%)	18	(0.05%)	50	(0.07%)	36	(0.15%)
Diabetes (treated)	317	(1.21%)	621	(1.63%)	1380	(1.98%)	543	(2.19%)
Gallbladder disease[3]	295	(1.12%)	467	(1.23%)	862	(1.23%)	295	(1.19%)
Hysterectomy[4]	127	(0.85%)	177	(0.77%)	323	(0.83%)	129	(0.95%)
Glaucoma	209	(0.80%)	384	(1.01%)	1128	(1.61%)	551	(2.22%)
Osteoporosis	412	(1.57%)	792	(2.08%)	2276	(3.26%)	1142	(4.60%)
Osteoarthritis[5]	773	(3.30%)	1469	(4.24%)	3672	(5.68%)	1671	(7.24%)
Rheumatoid arthritis	206	(0.78%)	357	(0.94%)	706	(1.01%)	282	(1.14%)
Intestinal polyps	339	(1.29%)	649	(1.71%)	1503	(2.15%)	607	(2.44%)
Lupus	40	(0.15%)	62	(0.16%)	125	(0.18%)	30	(0.12%)
Kidney Stones[5]	72	(0.44%)	131	(0.53%)	273	(0.56%)	88	(0.51%)
Cataracts[5]	291	(1.78%)	885	(3.55%)	3839	(7.88%)	2084	(12.06%)
Pills for hypertension	1612	(6.13%)	2959	(7.78%)	7114	(10.18%)	3186	(12.83%)

[1] Participants with unmarked ethnicity are classified as Minority.

[2] Inpatient DVT only.

[3] "Gallbladder disease" includes self-reports of both hospitalized and non-hospitalized events.

[4] Only women without a baseline hysterectomy are used to compute the annual rates of hysterectomy.

[5] These outcomes have not been self-reported on all versions of Form 33. The annualized percentages are corrected for the different amounts of follow-up.

Table 3.14
Sensitivity of DM Study Power to Adherence Assumptions

Outcome	Year	Intervention Effect[1] (%)	Percentage of Cases[1]		Power (%)		
			Control	Intervention	Design[2]	Revised Adherence[3]	Revised Goal[5]
Breast Cancer							
	2001	11	1.98	1.86	28	18	19
		12	1.99	1.85	35	22	23
		14	1.99	1.83	44	27	29
	2004	11	2.86	2.61	63	46	50
		12	2.86	2.57	75	56	62
		14	2.86	2.54	86[4]	67	73
Colorectal Cancer							
	2001	18	1.08	0.97	37	24	25
		20	1.08	0.96	45	28	30
		22	1.09	0.95	52	34	36
	2004	18	1.64	1.40	83	65	70
		20	1.63	1.37	90	75	80
		22	1.63	1.24	95	83	87

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

[2] C-I % Energy from fat: 13% at AV-1, 11% at year 10

[3] C-I % Energy from fat: 11% at AV-1, 9% at year 10. 8.5 follow-up years.

[4] Design values

[5] C-I % Energy from fat: 11% at AV-1, 10% at year 10. 8.5 follow-up years.

4. CaD Component

4.1 Recruitment

Table 4.1 presents the number of women randomized in the Calcium and Vitamin D component of the WHI Clinical Trial as of February 29, 2000. A total of 36,102 women have been randomized which is 80.2% of the overall goal of 45,000. The age distribution of the CaD trial participants is somewhat younger than anticipated in the design assumptions for the trial. Thus far, 17% of women randomized are aged 70-79 years compared with the design assumption of 25%.

4.2 Adherence

Table 4.2 presents rates of follow-up, stopping intervention and pill collection, and adherence to pill taking by visit schedule for all CaD participants, CaD participants randomized at AV-1 and CaD participants randomized at AV-2, respectively. The adherence pattern among women with pill collections is generally stable over time. The adherence summary for all CaD participants, defined as those women known to be consuming 80% or more of the prescribed dose, has improved since the last report and is now about 56%-63% (adherence summary was 55%-60% in the last progress report). Note that the adherence summary for AV-1 randomized CaD participants is somewhat higher at AV3 compared to participants randomized at AV-2 (59% vs. 51%) but this difference diminishes at AV4 and reverses at AV5. Adherence to CaD, however, remains somewhat low, primarily because of a significant proportion of women stopping the intervention entirely, and because of lower than expected pill-taking rates among women staying on the intervention.

Table 4.3 summarizes interval and cumulative drop-out rates in comparison to the original design assumptions. The original power calculations for CaD assumed a 6% drop-out rate in year 1 and a 3% per year drop-out rate thereafter. An independent lost-to-follow-up rate of 3% per year was also incorporated resulting in approximately 8.8% stopping intervention in year 1 and 5.9% in subsequent years. Our current data suggest the drop-out rates are somewhat higher than projected at AV2 and AV3, and then slightly lower (absolute difference of 1%) than projected at AV4 and AV5. By AV5, the observed and design-specified cumulative drop-out rates are very similar overall.

With this annual report, we have begun to summarize long-term trends in adherence and retention using survival models that incorporate data from the entire follow-up period rather than logistic models that look at incremental periods of follow-up. In the survival models, the outcome under study is time to first occurrence of non-adherence defined as taking <80% of study pills. Note that these models do not account for improvements in adherence after the first occurrence of non-adherence, but do provide information on the predictors of non-adherence that occurs anytime during the entire follow-up period. Table 4.4 is based on the entire CaD randomized cohort. Significant predictors of non-adherence include younger age (older women are less likely to be non-adherent); African-American or Latino race/ethnicity; non-married status, and reported symptoms of moderate/severe gas or bloating and/or constipation. Low education (0-8 years) and middle income (20-35K) were weakly associated with lower risk of non-adherence. Randomization in one of the other trials vs. both was not a significant predictor

of non-adherence. The four-week phone call appears to reduce risk of non-adherence by approximately 13%. Women who chose the swallowable formulation at randomization were at slightly greater risk of non-adherence (RR=1.06) than those women who chose chewable or who had no choice because they were randomized into CaD before swallowable pills became available. Modeling the choice of formulation over time, shown in the last column of *Table 4.4*, shows that choosing swallowable tablets was associated with a reduced risk of non-adherence (RR=0.84). The latter finding is shown in the last column of Table 4.4 which was based on a two-thirds sample of CaD participants. This finding is consistent with the interpretation that offering the choice of swallowable vs. chewable after randomization has improved adherence.

Table 4.5 summarizes the frequency of reported reasons for stopping CaD. The majority of women stopping study supplements do so of their own accord. Only 8-9% have indicated that they were advised by their physician to discontinue these supplements. Thirty-nine to forty-two percent of the women who have stopped taking their study pills report a reason related to the intervention itself, 26% report health reasons and 6% report personal reasons. Symptoms or health problems associated with the intervention was the most frequently reported intervention-related reason followed by not liking to take the pills.

We also monitor the number of women who have begun alternative anti-osteoporosis therapies within the CaD trial. As of February 29, 2000, 1003 (2.8%) women were taking alendronate, 139 (0.4%) were taking calcitonin, and 219 (0.6%) were taking raloxifene.

4.3 Bone Mineral Density

Table 4.6 presents the mean bone mineral density levels at AV-1 and AV-3 and percent change in BMD during this interval among women randomized at the three BMD measurement sites (Pittsburgh, Arizona, Birmingham). At the three skeletal sites examined (hip, spine, and whole body), BMD has increased between AV-1 and AV-3 from 1.3-1.5%, with the greatest change occurring at the spine.

4.4 Vital Status

Table 4.7 presents data on the vital status and the participation status of participants in the CaD trial. A detailed description of CCC and clinic activities to actively locate participants who do not complete their periodic visits is given in *Section 5 – Outcomes*. For operational purposes, we define CT participants to have an "unknown" participation status if there is no outcomes information from the participant for 18 months, and no other contacts for 6 months. Currently 1.1% of the participants are lost-to-follow-up or have stopped follow-up, and 0.7% of the participants are known to be deceased. Virtually all of the remaining participants have completed a *Form 33 – Medical History Update* in the last 18 months. The design assumed that 3% per year would be lost to follow-up or death. Currently the average follow-up for CaD participants is about 2.0 years, suggesting that approximately 5.9% could be expected to be dead or lost to follow-up. Our overall rates compare favorably to design assumptions.

4.5 Outcomes

Table 4.8 contains counts of the number of locally verified major WHI outcomes for CaD participants. In this table only outcomes that took place after randomization in the CaD trial are included. Approximately 10-15% of the self-reported outcomes have not yet been verified, so the numbers in this table should thus be seen as a lower bound to the actual number of outcomes that took place. Currently we have only observed about 30% of the number of hip fractures that we expected in the power calculations to have observed with the current follow-up. The number of observed colorectal and breast cancer cases is approximately 90-100% of what was expected. The number of CHD events is about 75% of what was expected.

Table 4.9 contains counts of the number of self-reports for some outcomes that are not locally verified in WHI. As most of the self-reported outcomes are somewhat over-reported (see *Section 6.3 – Outcomes Data Quality*), the number in this table should be taken as an upper bound to the number of events that have occurred in CaD participants.

4.6 Power Considerations

Since significant proportions of still active women are taking less than the prescribed dose, it is anticipated that this would have an additional effect on study power beyond drop-out rates. To examine these effects, we have calculated the power for CaD using the type of adherence model employed for the DM component. This approach incorporates total calcium intake from diet and supplements. To make within-model comparisons, we determined the calcium intake assumptions that would reproduce the original power calculations based on a model that dichotomized adherence to pills, holding constant all other parameters (e.g., treatment effect, lag time, control group incidence rates, and average follow-up time). Total calcium consumption (in mg) of 920, 950, 1000 at baseline, year 1 and year 9, respectively in controls and similarly 1920, 1850, 1800 in the intervention arm produces powers within 1%-2% of the protocol-specified values with n=45,000 for all outcomes of interest. The value of 920 mg/day in controls at baseline was determined from the median total calcium intake in the CaD participants at AV-1 who are also DM participants, and who therefore provide FFQ data.

With recruitment ongoing we have conducted power sensitivity analyses using a projected sample size of 36,000, an adherence pattern suggested by the current data and revised incidence rates, reflecting the low early rates of hip fractures (healthy volunteer effect starting at 0.2 in year 1 and rising to 0.8 by year 7). *Table 4.10* shows the power for Hip Fractures, Other Fractures and colorectal cancer under both adherence patterns and all other parameters held constant. Note that power is low for hip fracture and colorectal cancer in scenarios based on poor adherence. Power for all clinical fractures is high under most scenarios, especially if moderate adherence is achieved.

4.7 Issues

We continue to direct efforts towards improving adherence to Calcium-Vitamin D study medication. On May 19th-20th, 2000 a workshop will take place to address adherence and safety issues in the HRT and CaD trials. This workshop will include training to enhance interpersonal skills (e.g., motivational interviewing skills) to re-motivate participants in both medication trials; instruction on the use of a new triaging system to improve participant adherence;

practical management strategies to assist with adherence programs such as use of WHILMA reports and symptom management in the CaD trial; discussion of safety issues related to CaD; relevant scientific updates; and use of available forms and data related to adherence and retention.

In February 2000, the safe upper limit of personal vitamin D intake allowed by the WHI protocol increased from 600 IU per day to 1000 IU per day. WHI participants in the CaD trial who also take their own calcium-Vitamin D supplements were sometimes having Vitamin D intakes in excess of the 600 IU limit, and clinics were obligated under the old protocol to advise participants to discontinue study medication for safety reasons. However, in 1997 the Institute of Medicine set a safe, tolerable upper limit for Vitamin D of 2000 IU per day. This protocol change should allow us to avoid adherence problems arising from intake of Vitamin D from personal supplements, and still allows a significant margin of safety.

The BMD UCSF Coordinating Center (CCC subcontractor) was asked to investigate the positive changes in BMD being observed in the WHI program overall, as evidenced by the positive changes in the OS cohort. Issues of quality assurance, calibration and potential drift are being investigated with collaborative oversight by the CaD/Osteoporosis Advisory Committee and the CCC. It is anticipated that evaluation of BMD data from Year 3 of the program will be instrumental in evaluating these trends and identifying if any corrective action is needed.

Table 4.1
Calcium and Vitamin D Component Age - Specific Recruitment

Data as of: February 29, 2000

	Total Randomized	% of Overall Goal	Age Distribution	Design Assumption
CaD	**36,102**			
50-54	5157	118%	14%	10
55-59	8254	94%	23%	20
60-69	16,401	83%	45%	45
70-79	6290	58%	17%	25

Table 4.2
CaD Adherence Summary
All CaD Participants

Data as of: February 29, 2000

	Due	Conducted		Conducted in Window		Stopped CaD		Missed Pill Collection		Total with Collections		Medication Rate[1] <50%		Medication Rate[1] 50%-80%		Medication Rate[1] 80% +		Adherence Summary[2]
	N	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	%
Semi-Annual Contact-2	33013	32136	97	26140	79	2115	6	4208	13	28778	87	4057	14	5762	20	18959	66	58
Annual Visit-2	30541	29700	97	24065	79	1353	4	2135	8	25821	92	2670	10	4424	17	18727	73	62
Annual Visit -3	22636	21711	96	17234	76	1556	7	2079	10	17892	90	1640	9	3167	18	13085	73	58
Annual Visit -4	11381	10798	95	8532	75	554	5	831	9	8433	91	660	8	1364	16	6409	76	57
Annual Visit -5	4342	4099	94	3336	77	207	5	280	8	3109	92	208	7	439	14	2462	79	57

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

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

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

Table 4.2 (continued)
CaD Adherence Summary
Participants Randomized to CaD at Annual Visit 1 (AV-1)

Data as of: February 29, 2000

	Due	Stopped CaD		Missed Pill Collection		Total with Collections		Medication Rate[1] <50%		Medication Rate[1] 50%-80%		Medication Rate[1] 80% +		Adherence Summary[2]
	N	N	%	N	%	N	%	N	%	N	%	N	%	%
Annual Visit-2	30461	1353	4	2134	8	25815	92	2669	10	4423	17	18723	73	62
Annual Visit -3	20406	1282	6	1729	10	16124	90	1376	9	2762	17	11986	74	59
Annual Visit -4	9940	473	5	730	9	7418	91	550	7	1185	16	5683	77	57
Annual Visit -5	3107	151	5	223	9	2198	91	141	6	313	14	1744	79	56

[1] Medication rate calculated as the number of pills taken divided by the number of days since bottle(s) were dispensed.
[2] Adherence summary calculated as the number of women consuming ≥80% of pills divided by the number due for a visit.
Note: Deceased women are excluded from all medication adherence calculations.

Table 4.2 (continued)
CaD Adherence Summary
Participants Randomized to CaD at Annual Visit 2 (AV-2)

Data as of: February 29, 2000

	Due	Stopped CaD		Missed Pill Collection		Total with Collections		Medication Rate[1] <50%		Medication Rate[1] 50%-80%		Medication Rate[1] 80% +		Adherence Summary[2]
	N	N	%	N	%	N	%	N	%	N	%	N	%	%
Annual Visit -3	2064	269	13	346	17	1713	83	258	15	395	23	1060	62	51
Annual Visit -4	1328	81	6	100	9	1011	91	109	11	179	18	723	72	54
Annual Visit -5	1179	56	5	57	6	911	94	67	7	126	14	718	79	61

[1] Medication rate calculated as the number of pills taken divided by the number of days since bottle(s) were dispensed.
[2] Adherence summary calculated as the number of women consuming ≥80% of pills divided by the number due for a visit.
Note: Deceased women are excluded from all medication adherence calculations.

Table 4.3
CaD Drop-Out Rates by Follow-Up Time
(Design-specified values in parentheses)

Data as of: February 29, 2000

	Total			
	Interval[1]		Cumulative[2]	
Drop-Outs[3]				
AV-2	10.5%	(8.8)	10.5%	(8.8)
AV-3	6.9%	(5.9)	16.7%	(14.2)
AV-4	4.9%	(5.9)	20.8%	(19.2)
AV-5	4.8%	(5.9)	24.6%	(24.0)

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

[2] Estimates of cumulative rates.

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

Table 4.4
Cox Proportional Hazards Model Analysis of CaD Medication Adherence: Time to First Non-Adherent Visit[1]

Data as of: February 29, 2000

	CaD (N=36102)			
	Non-Adherent[2] Participants (N=16422)	Adherent Participants (N=19680)	Hazard Ratio for non-adherence[3] All Data	Hazard Ratio for non-adherence[3] 2/3 Subsample
Age:				
50-54[4]	2885	2272	1.00	1.00
55-59	4073	4183	0.93 **	0.95
60-69	6769	9629	0.84 **	0.87 **
70-79	2695	3596	0.90 **	0.92 *
Ethnicity:				
White	13176	16840	1.00	1.00
Black	1880	1412	1.45 **	1.44 **
Hispanic	800	695	1.24 **	1.20 **
Other Minority	566	733	1.07	1.12 *
Education:				
0-8 Years	283	243	0.96 *	0.96
Some H.S. / Diploma	3506	4501	1.06	1.06
Post H.S.	12524	14813	1.00	1.00
Income:				
<20 K	2769	3018	1.00	1.00
20-35K	3926	4941	0.95 *	0.95
35K-50K	3286	3983	0.98	0.96
>50K	5612	6732	0.98	0.98
Marital Status:				
Married	9964	12281	1.00	1.00
Not Married	6392	7324	1.05 **	1.07 **
Four Week Phone Call[5]:				
No	6161	4819	1.00	1.00
Yes	10261	14861	0.87 **	0.92 **
Gas:				
Symptom Did Not Occur	5476	6813	1.00	1.00
Mild	7977	9939	1.00	0.99
Moderate to Severe	2969	2928	1.12 **	1.14 **
Constipation:				
Symptom Did Not Occur	10756	13422	1.00	1.00
Mild	4262	4924	1.04 *	1.04
Moderate to Severe	1404	1334	1.12 **	1.12 **
Primary CT Randomization:				
DM and HRT	2396	2614	1.00	1.00
HRT only	4804	6220	0.98	1.00
DM only	9222	10846	0.99	1.01
CaD Formulation:[6]				
Chewable	5594	5996	1.00	1.00
Swallowable	10822	13677	1.06 **	0.84 **

[1] * P-values <=.05 from Wald Test; ** P-values <=.01 from Wald Test.

[2] Non-adherence defined as participants who took less than 80% of CaD medications, stopped intervention, or were lost to follow-up.

[3] Due to programming limitations, model with time-dependent covariate run on a 2/3 random subsample.

[4] Underlined levels are reference categories.

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

[6] Formulation at randomization in table and all data; included as a time-dependent covariate in 2/3 subsample.

Table 4.5
Reasons for Stopping CaD

Data as of: February 29, 2000

Reasons[1]	(N=5968)	
Personal	374	(6%)
Travel	144	(2%)
Study Procedures	87	(1%)
Health	1539	(26%)
Experiencing health problems or symptoms not due to intervention	861	(14%)
Worried about health effects of medical tests	28	(<1%)
Worried about costs if adverse effects occur	11	(<1%)
Advised not to participate by health care provider	505	(8%)
Study conflicts with health care needs	393	(7%)
Expected more care	17	(<1%)
Intervention	2411	(40%)
Reports health problems or symptoms from WHI Intervention	1562	(26%)
Problem with Clinic Practitioner or other CC staff	5	(<1%)
Doesn't like taking pills	690	(12%)
Doesn't like DM requirements	13	(<1%)
Problems with DM group nutritionist or group members	4	(<1%)
Doesn't like DM eating patterns	5	(<1%)
Doesn't like randomized nature of intervention	267	(4%)
Expected some benefit from intervention	47	(1%)
Won't participate in safety procedures	44	(1%)
Other	1883	(32%)
Not Given	752	(13%)

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

Table 4.6
Bone Mineral Density[1] Analysis: CaD Participants

Data as of: February 29, 2000

	N	Mean	S.D.
Whole Body Scan			
AV1	2434	1.02	0.11
AV3	1878	1.04	0.11
AV3 % Change from baseline BMD[2]	1806	1.41	3.31
Spine Scan			
AV1	2372	0.99	0.16
AV3	1846	1.01	0.17
AV3 % Change from baseline BMD[2]	1774	1.54	4.27
Hip Scan			
AV1	2426	0.86	0.14
AV3	1874	0.88	0.14
AV3 % Change from baseline BMD[2]	1805	1.34	3.57

[1] Measured in (g/cm^2).

[2] Percent Change from BMD is defined as ((AV3-AV1)/AV1)x100

Table 4.7
Lost-to-Follow-up and Vital Status: CaD Participants

Data as of: February 29, 2000

	CaD Participants (N=36102)	
	N	%
Vital Status/Participation		
Deceased	258	0.7
Alive: Current Participation[1]	34820	96.4
Alive: Recent Participation[2]	615	1.7
Alive: Past/Unknown Participation[3]	6	<0.1
Stopped Follow-Up[4]	176	0.5
Lost to Follow-Up[5]	227	0.6

[1] Participants who have filled in a Form 33 within the last 9 months.
[2] Participants who last filled in a Form 33 between 9 and 18 months ago.
[3] Participiants without a Form 33 within the last 18 months, who have been located (as indicated on Form 23) within the last 6 months.
[4] Participants with codes 5 (no follow-up) or 8 (absolutely no follow-up) on Form 7.
[5] Participants not in any of the above categories.

Table 4.8
Locally Verified Outcomes (Annualized Percentages) by Ethnicity for Calcium and Vitamin D

Data as of: February 29, 2000

Outcomes	Total		Minority[1]		White	
No. of participants w/ *Form 33*	35454		5910		29544	
Mean follow-up (months)	24.4		23.0		24.7	
Fractures						
Hip fracture	47	(0.07%)	2	(0.02%)	45	(0.07%)
Vertebral fracture	63	(0.09%)	6	(0.05%)	57	(0.09%)
Other fracture[5,2]	993	(1.38%)	93	(0.82%)	900	(1.48%)
Total fracture	1078	(1.50%)	100	(0.88%)	978	(1.61%)
Cancer						
Colorectal cancer	93	(0.13%)	18	(0.16%)	75	(0.12%)
Breast cancer[3]	321	(0.45%)	31	(0.27%)	290	(0.48%)
Invasive breast cancer	248	(0.34%)	26	(0.23%)	222	(0.37%)
In situ breast cancer	72	(0.10%)	5	(0.04%)	67	(0.11%)
Ovary cancer	34	(0.05%)	4	(0.04%)	30	(0.05%)
Endometrial Cancer[4]	47	(0.11%)	3	(0.05%)	44	(0.12%)
Other cancer[5,6]	317	(0.44%)	29	(0.26%)	288	(0.47%)
Total cancer	800	(1.11%)	85	(0.75%)	715	(1.18%)
Cardiovascular						
CHD[7]	216	(0.30%)	27	(0.24%)	189	(0.31%)
Coronary death	61	(0.08%)	10	(0.09%)	51	(0.08%)
Total MI[8]	166	(0.23%)	18	(0.16%)	148	(0.24%)
Clinical MI	156	(0.22%)	15	(0.13%)	141	(0.23%)
Definite Silent MI	16	(0.02%)	3	(0.03%)	13	(0.02%)
Possible Silent MI	48	(0.07%)	10	(0.09%)	38	(0.06%)
Angina	290	(0.40%)	37	(0.33%)	253	(0.42%)
CABG/PTCA	242	(0.34%)	28	(0.25%)	214	(0.35%)
Carotid artery disease	55	(0.08%)	4	(0.04%)	51	(0.08%)
Congestive heart failure	148	(0.21%)	21	(0.19%)	127	(0.21%)
Stroke	141	(0.20%)	20	(0.18%)	121	(0.20%)
PVD	35	(0.05%)	8	(0.07%)	27	(0.04%)
CHD[7]/Possible Silent MI	260	(0.36%)	37	(0.33%)	223	(0.37%)
Coronary disease[9]	630	(0.87%)	85	(0.75%)	545	(0.90%)
Total CVD	858	(1.19%)	117	(1.03%)	741	(1.22%)
Deaths						
Cardiovascular deaths	75	(0.10%)	11	(0.10%)	64	(0.11%)
Cancer deaths	100	(0.14%)	12	(0.11%)	88	(0.14%)
Deaths: other known cause	26	(0.04%)	3	(0.03%)	23	(0.04%)
Deaths: unknown cause	10	(0.01%)	4	(0.04%)	6	(0.01%)
Deaths: not yet adjudicated	47	(0.07%)	13	(0.11%)	34	(0.06%)
Total death	258	(0.36%)	43	(0.38%)	215	(0.35%)

[1] Participants with unmarked ethnicity are classified as Minority.

[2] "Other fracture" excludes fractures indicated as pathological.

[3] Excludes four cases with borderline malignancy.

[4] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

[5] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[6] Excludes non-melanoma skin cancer

[7] "CHD" includes clinical MI, definite silent MI, and coronary death.

[8] "Total MI" includes clinical MI and definite silent MI.

[9] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina,congestive heart failure, and CABG/PTCA.

Table 4.8
Locally Verified Outcomes (Annualized Percentages) by Age for Calcium and Vitamin D

Data as of: February 29, 2000

Outcome	50-54		55-59		60-69		70-79	
No. of participants w/ *Form 33*	5105		8168		16021		6160	
Mean follow-up (months)	29.7		26.0		22.7		22.1	
Fractures								
Hip fracture	3	(0.02%)	5	(0.03%)	16	(0.05%)	23	(0.20%)
Vertebral fracture	2	(0.02%)	6	(0.03%)	28	(0.09%)	27	(0.24%)
Other fracture[1,4]	140	(1.11%)	214	(1.21%)	440	(1.45%)	199	(1.75%)
Total fracture	144	(1.14%)	223	(1.26%)	473	(1.56%)	238	(2.10%)
Cancer								
Colorectal cancer	8	(0.06%)	18	(0.10%)	39	(0.13%)	28	(0.25%)
Breast cancer[2]	44	(0.35%)	82	(0.46%)	143	(0.47%)	52	(0.46%)
Invasive breast cancer	33	(0.26%)	63	(0.36%)	115	(0.38%)	37	(0.33%)
In situ breast cancer	11	(0.09%)	19	(0.11%)	28	(0.09%)	14	(0.12%)
Ovary cancer	4	(0.03%)	9	(0.05%)	14	(0.05%)	7	(0.06%)
Endometrial Cancer[3]	7	(0.10%)	11	(0.10%)	22	(0.12%)	7	(0.11%)
Other cancer[4,5]	31	(0.25%)	60	(0.34%)	148	(0.49%)	78	(0.69%)
Total cancer	94	(0.74%)	176	(0.99%)	360	(1.19%)	170	(1.50%)
Cardiovascular								
CHD[6]	19	(0.15%)	24	(0.14%)	107	(0.35%)	66	(0.58%)
Coronary death	4	(0.03%)	5	(0.03%)	32	(0.11%)	20	(0.18%)
Total MI[7]	16	(0.13%)	19	(0.11%)	81	(0.27%)	50	(0.44%)
Clinical MI	14	(0.11%)	19	(0.11%)	75	(0.25%)	48	(0.42%)
Silent MI	3	(0.02%)	0	(0.00%)	9	(0.03%)	4	(0.04%)
Possible Silent MI	7	(0.06%)	10	(0.06%)	15	(0.05%)	16	(0.14%)
Angina	23	(0.18%)	36	(0.20%)	135	(0.45%)	96	(0.85%)
CABG/PTCA	17	(0.13%)	28	(0.16%)	111	(0.37%)	86	(0.76%)
Carotid artery disease	2	(0.02%)	5	(0.03%)	24	(0.08%)	24	(0.21%)
Congestive heart failure	6	(0.05%)	21	(0.12%)	64	(0.21%)	57	(0.50%)
Stroke	5	(0.04%)	18	(0.10%)	62	(0.20%)	56	(0.49%)
PVD	1	(0.01%)	2	(0.01%)	14	(0.05%)	18	(0.16%)
CHD[6]/Possible Silent MI	26	(0.21%)	33	(0.19%)	122	(0.40%)	79	(0.70%)
Coronary disease[8]	47	(0.37%)	81	(0.46%)	288	(0.95%)	214	(1.89%)
Total CVD	57	(0.45%)	107	(0.60%)	404	(1.33%)	290	(2.56%)
Deaths								
Cardiovascular deaths	4	(0.03%)	6	(0.03%)	36	(0.12%)	29	(0.26%)
Cancer deaths	5	(0.04%)	14	(0.08%)	47	(0.15%)	34	(0.30%)
Deaths: other known cause	2	(0.02%)	4	(0.02%)	11	(0.04%)	9	(0.08%)
Deaths: unknown cause	0	(0.00%)	2	(0.01%)	4	(0.01%)	4	(0.04%)
Deaths: not yet adjudicated	8	(0.06%)	3	(0.02%)	20	(0.07%)	16	(0.14%)
Total death	19	(0.15%)	29	(0.16%)	118	(0.39%)	92	(0.81%)

[1] "Other fracture" excludes fractures indicated as pathological.

[2] Excludes four cases with borderline malignancy.

[3] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

[4] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[5] Excludes non-melanoma skin cancer

[6] "CHD" includes clinical MI, definite silent MI, and coronary death.

[7] "Total MI" includes clinical MI and definite silent MI.

[8] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

Table 4.9
Counts (Annualized Percentages) of Participants with Self-Reported Outcomes by Ethnicity and Age for Calcium and Vitamin D

Data as of: February 29, 2000

Outcomes	Total	Ethnicity: Minority[1]	Ethnicity: White
No. of participants w/ *Form 33*	35454	5910	29544
Mean follow-up (months)	24.4	23.0	24.7
Hospitalizations			
Ever	6134 (8.52%)	914 (8.08%)	5220 (8.60%)
Two or more	1829 (2.54%)	273 (2.41%)	1556 (2.56%)
Other			
DVT[2]	138 (0.19%)	11 (0.10%)	127 (0.21%)
PE	57 (0.08%)	8 (0.07%)	49 (0.08%)
Diabetes (treated)	1681 (2.33%)	579 (5.12%)	1102 (1.82%)
Gallbladder disease[3]	965 (1.34%)	145 (1.28%)	820 (1.35%)
Hysterectomy[4]	354 (0.84%)	36 (0.65%)	318 (0.87%)
Glaucoma	1159 (1.61%)	269 (2.38%)	890 (1.47%)
Osteoporosis	2249 (3.12%)	283 (2.50%)	1966 (3.24%)
Osteoarthritis[5]	4075 (6.12%)	770 (7.25%)	3305 (5.90%)
Rheumatoid arthritis	738 (1.02%)	257 (2.27%)	481 (0.79%)
Intestinal polyps	1549 (2.15%)	241 (2.13%)	1308 (2.15%)
Lupus	150 (0.21%)	20 (0.18%)	130 (0.21%)
Kidney Stones[5]	237 (0.49%)	45 (0.59%)	192 (0.47%)
Cataracts[5]	4118 (8.44%)	677 (8.85%)	3441 (8.37%)
Pills for hypertension	8339 (11.58%)	1983 (17.53%)	6356 (10.47%)

Outcome	Age: 50-54	55-59	60-69	70-79
Number randomized	5105	8168	16021	6160
Mean follow-up (months)	29.7	26.0	22.7	22.1
Hospitalizations				
Ever	730 (5.78%)	1222 (6.90%)	2818 (9.29%)	1364 (12.03%)
Two or more	201 (1.59%)	318 (1.79%)	838 (2.76%)	472 (4.16%)
Other				
DVT[2]	9 (0.07%)	27 (0.15%)	65 (0.21%)	37 (0.33%)
PE	4 (0.03%)	11 (0.06%)	28 (0.09%)	14 (0.12%)
Diabetes (treated)	226 (1.79%)	401 (2.26%)	743 (2.45%)	311 (2.74%)
Gallbladder disease[3]	146 (1.16%)	253 (1.43%)	421 (1.39%)	145 (1.28%)
Hysterectomy[4]	55 (0.76%)	85 (0.78%)	161 (0.91%)	53 (0.83%)
Glaucoma	120 (0.95%)	206 (1.16%)	553 (1.82%)	280 (2.47%)
Osteoporosis	201 (1.59%)	404 (2.28%)	1081 (3.56%)	563 (4.96%)
Osteoarthritis[5]	449 (3.93%)	835 (5.12%)	1877 (6.66%)	914 (8.59%)
Rheumatoid arthritis	103 (0.82%)	193 (1.09%)	316 (1.04%)	126 (1.11%)
Intestinal polyps	178 (1.41%)	331 (1.87%)	741 (2.44%)	299 (2.64%)
Lupus	28 (0.22%)	36 (0.20%)	66 (0.22%)	20 (0.18%)
Kidney Stones[5]	26 (0.33%)	63 (0.54%)	111 (0.52%)	37 (0.47%)
Cataracts[5]	196 (2.50%)	568 (4.85%)	2127 (10.03%)	1227 (15.47%)
Pills for hypertension	965 (7.65%)	1719 (9.70%)	3798 (12.52%)	1857 (16.38%)

[1] Participants with unmarked ethnicity are classified as Minority.

[2] Inpatient DVT only.

[3] "Gallbladder disease" includes self-reports of both hospitalized and non-hospitalized events.

[4] Only women without a baseline hysterectomy are used to compute the annual rates of hysterectomy.

[5] These outcomes have not been self-reported on all versions of Form 33. The annualized percentages are corrected for the different amounts of follow-up.

Table 4.10
Sensitivity of CaD Study Power to Adherence and Incidence Rate Assumptions
Revised Sample Size of 36,000

	Year	Intervention Effect[1] (%)	Percentage of Cases[1] Control	Intervention	Design[2]	Revised Assumptions[3]
Hip Fractures						
	2001	20	1.61	1.36	57	29
		27	1.62	1.31	74	40
		33	1.62	1.26	86	52
	2004	20	2.84	2.35	86	58
		27	2.85	2.25	96	75
		33	2.85	2.15	99	88
Combined Fractures						
	2001	19	6.48	5.54	98	91
		23	6.50	5.36	>99	98
		28	6.51	5.18	>99	>99
	2004	19	10.22	8.62	>99	99
		23	10.24	8.30	>99	>99
		28	10.25	7.98	>99	>99
Colorectal Cancer						
	2001	18	0.90	0.80	22	15
		20	0.90	0.79	26	18
		22	0.90	0.78	30	20
	2004	18	1.48	1.22	68	47
		20	1.49	1.20	77	54
		22	1.49	1.18	84	62

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

[2] For design, the calculations were based on n = 35,000.

[3] For revised assumption, calculations were based on n = 36,000 and 7.5 years of follow-up for years 1 though 9. For hip fractures, healthy volunteer factors of (.20, .30, .40, .50, .60, .70, .80, .80, .80) were applied to the incidence rates for follow-up years 1 through 9.

5. Observational Study

5.1 Recruitment

Recruitment into the OS component, completed in December of 1998, reached 93,721, approximately 94% of the expected sample size. *Table 5.1* documents the age distribution and the racial/ethnic composition of this cohort.

5.2 Overview of Follow-up

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

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

5.3 Completeness of Annual Mail Follow-up

Table 5.2 shows completeness of OS mail follow-up by follow-up year, type of contact, and clinic group. These rates include participants for whom the full sequence of mailings are complete and there has been at least two months for CC follow-up of non-responders.

The overall response of 95.8% for year 1 data collection, which includes mailings plus CC follow-up of non-responders, slightly exceeds the 95% goal for completion of the OS Exposure Update (*Form 48*), but falls short of the optimal goal (98%) for completion of the Medical History Update (*Form 33*). For years 2 and 4, the rates fall slightly short of the 94% (Y2) and 92% (Y4) goals for the Exposure Update, at least in part because CC follow-up of non-responders is not required in even numbered follow-up years.

5.4 Completeness of Year 3 Clinic Visit

Table 5.3 shows completeness of activities conducted at the year 3 clinic visit. Of those participants due for the year 3 visit through 4/30/99, 94% overall completed medical history updates (*Form 33*) and 83% provided blood samples (*Form 100*).

5.5 Bone Mineral Density

Bone scans are given to all enrolled WHI participants in three Clinical Centers: Birmingham, Pittsburgh and Tucson. The choice of three centers was based on reducing the variability associated with multiple sites and operators while achieving adequate sample size. The selection of these three Clinical Centers was based both on their previous experience in bone densitometry and the expected enrollment of minorities which will allow us to address hypotheses regarding racial/ethnic differences. Bone scans are given at baseline and years 1, 3, 6, and 9 in these centers.

Table 5.4 shows the OS component-specific BMD means and standard deviations for baseline AV-3 along with % change from baseline for the three types of scans available: whole body, spine, and hip. Baseline and % change is also given using only those women who have an AV3 bone scan, as nearly 3,000 of the women with a baseline do not have an AV3 measure. The current data suggest overall a very small increase in bone density over three years in this group of women. In general, we would have expected a small decrease in BMD over time. As with the corresponding DM results, this increase could be related to some selection of health conscious women who may be taking hormone replacement therapy or calcium supplements of their own. Alternatively, there may be some bias introduced by missing data (currently 33% of OS women at these 3 sites are missing BMD data) or there may be a measurement problem. Further investigation of this issue is needed.

5.6 Vital Status

Table 5.5 presents data on the vital status and the participation status of participants in the OS. A detailed description of CC and CCC activities to actively locate participants who do not complete their periodic visits is given in *Section 6 – Outcomes*. For operational purposes, we define OS participants to be lost to follow-up if there is no outcomes information from the participant for 24 months. Currently 1.9% of the participants are lost to follow-up, and an additional 0.6% of the participants have stopped follow-up. About 1.2% of the OS participants are deceased. Note that some OS participants have been in the study for fewer than 24 months. Those participants would be classified in the "current participation" or the "recent participation" categories even if they never filed a *Form 33*.

5.7 Outcomes

Table 5.6 contains counts of the number of locally verified major WHI outcomes for OS participants by age and ethnicity. Approximately 10-15% of the self-reported outcomes have not yet been verified, the numbers in this table can be seen as a lower bound to the actual number of outcomes that took place. Compared to the incidence rates used in the CT design. we have slightly more than 100% of the expected number of breast cancers, 60% of the expected number of colorectal cancers, about 40% of the expected number of CHD events, and about 30% of the expected number hip fractures.

Table 5.7 contains counts of the number of self-reports for some outcomes that are not locally verified in WHI. As most of the locally verified outcomes are somewhat over-reported (see *Section 6.3 – Outcomes Data Quality*), the number in this table should be taken as an upper bound to the number of events that have occurred among OS participants.

Table 5.1
Observational Study Age and Ethnicity Specific Recruitment

Data as of: February 29, 2000

	Total Randomized	Distribution
Age	**93,721**	
50-54	12384	13%
55-59	17327	18%
60-69	41215	44%
70-79	22795	24%
Ethnicity	**93,721**	
American Indian	422	<1%
Asian	2671	3%
Black	7639	8%
Hispanic	3649	4%
White	78024	83%
Other/Unspecified	1316	1%

Table 5.2
Response Rates to OS Follow-up Procedures

Data as of: February 29, 2000

	# Due[1]	Mailings Initiated[2] N	Mailings Initiated[2] %	Response to Mailings N	Response to Mailings %[3]	Response to CC follow-up N	Response to CC follow-up %[4]	Total Responses N	Total Responses %[5]
Year 1	76003	75832	99.8	70459	92.9	2325	43.3	72784	95.8
VCC	34342	34315	99.9	31611	92.1	1483	54.9	33094	96.4
NCC	41661	41517	99.7	38848	93.6	842	31.6	39690	95.3
Year 2	54932	53540	97.5	50418	94.2	N/A		50916	92.7
VCC	25952	25288	97.4	23798	94.1	N/A		24134	93.0
NCC	28980	28252	97.5	26620	94.2	N/A		26782	92.4
Year 4	2626	2514	95.7	2371	94.3	N/A		2391	91.1
VCC	2595	2484	95.7	2343	94.3	N/A		2362	91.1
NCC	31	30	96.8	28	93.3	N/A		29	93.5

[1] Excludes women who are deceased.
[2] Mailings are not sent to women who have requested no follow-up, who are deceased, who have a non-deliverable address at the time of mailing, or who have a *Form 33* completed within the previous 3 months.
[3] Percent response of those initiated.
[4] Percent response from OS participants not responding to mailings. CC follow-up not required in even numbered follow-up years.
[5] Percent response of those due.

Table 5.3
OS Annual Visit 3 Task Completeness

Data as of: February 29, 2000

Task	# Due[1]	# Done[2]	% Done
Form 33 – Medical History Update	32086	30223	94%
Form 38 – Daily Life	32086	28151	88%
Form 44 – Current Medications	32086	27265	85%
Form 45 – Current Supplements	32086	27217	85%
Form 80 – Physical Measures	32086	26871	84%
Form 100 – Blood Collection	32086	26637	83%
Form 143 – Follow-up	32086	28014	87%

[1] Excludes women who are deceased.
[2] Tasks completed within –3/+10 month window.

Table 5.4
Bone Mineral Density Analysis: OS Participants

Data as of: February 29, 2000

	N	Mean	S.D.
Whole Body Scan			
Baseline[1]	6419	1.01	0.11
Baseline (for ppts. with an AV3 scan)	4149	1.01	0.11
AV3	4177	1.02	0.11
AV3 % Change from baseline BMD[2]	4149	1.11	3.64
Spine Scan			
Baseline	6312	0.98	0.17
Baseline (for ppts. with an AV3 scan)	4075	0.98	0.17
AV3	4096	0.99	0.18
AV3 % Change from baseline BMD	4075	1.79	5.14
Hip Scan			
Baseline	6418	0.84	0.14
Baseline (for ppts. with an AV3 scan)	4158	0.84	0.14
AV3	4175	0.85	0.14
AV3 % Change from baseline BMD	4158	0.84	4.28

[1] Measured in (g/cm^2).
[2] AV3 % Change from baseline BMD is defined as ((AV3-Baseline)/Baseline)x100

Table 5.5
Lost-to-Follow-up and Vital Status: OS Participants

Data as of: February 29, 2000

	OS Participants (N=93721)	
	N	%
Vital Status/Participation		
Deceased	1097	1.2
Alive: Current Participation[1]	85797	91.5
Alive: Recent Participation[2]	4362	4.7
Alive: Past/Unknown Participation[3]	129	0.1
Stopped Follow-Up[4]	552	0.6
Lost to Follow-Up[5]	1784	1.9

[1] Participants who have filled in a Form 33 within the last 15 months.
[2] Participants who last filled in a Form 33 between 15 and 24 months ago.
[3] Participants without a Form 33 within the last 18 months, who have been located (as indicated on Form 23) within the last 6 months.
[4] Participants with codes 5 (no follow-up) or 8 (absolutely no follow-up) on Form 7.
[5] Participants not in any of the above categories.

Table 5.6
Locally Verified Outcomes (Annualized Percentages) by Ethnicity for Observational Study

Data as of: February 29, 2000

Outcomes	Total		Ethnicity: Minority[1]		White	
Number enrolled	93721		15697		78024	
Mean follow-up (months)	31.5		29.4		31.9	
Cardiovascular						
CHD[2]	491	(0.20%)	62	(0.16%)	429	(0.21%)
Coronary death	103	(0.04%)	12	(0.03%)	91	(0.04%)
Clinical MI	417	(0.17%)	54	(0.14%)	363	(0.18%)
Angina	986	(0.40%)	123	(0.32%)	863	(0.42%)
CABG/PTCA	784	(0.32%)	89	(0.23%)	695	(0.34%)
Carotid artery disease	181	(0.07%)	22	(0.06%)	159	(0.08%)
Congestive heart failure	474	(0.19%)	75	(0.20%)	399	(0.19%)
Stroke	391	(0.16%)	72	(0.19%)	319	(0.15%)
PVD	128	(0.05%)	15	(0.04%)	113	(0.05%)
Coronary disease[3]	1763	(0.72%)	227	(0.59%)	1536	(0.74%)
Total CVD	2296	(0.93%)	314	(0.82%)	1982	(0.96%)
Cancer						
Breast cancer[4]	1125	(0.46%)	123	(0.32%)	1002	(0.48%)
Invasive breast cancer	915	(0.37%)	92	(0.24%)	823	(0.40%)
In situ breast cancer	213	(0.09%)	30	(0.08%)	183	(0.09%)
Ovary cancer	104	(0.04%)	10	(0.03%)	94	(0.05%)
Endometrial Cancer[5]	145	(0.10%)	16	(0.08%)	129	(0.10%)
Colorectal cancer	238	(0.10%)	38	(0.10%)	200	(0.10%)
Other cancer[6,7]	988	(0.40%)	85	(0.22%)	903	(0.44%)
Total cancer	2559	(1.04%)	266	(0.69%)	2293	(1.11%)
Fractures						
Hip fracture	206	(0.08%)	9	(0.02%)	197	(0.10%)
Vertebral fracture[8]	37	(0.17%)	2	(0.04%)	35	(0.20%)
Other fracture[6,8,9]	293	(1.31%)	30	(0.62%)	263	(1.50%)
Total fracture[10]	526	(0.21%)	41	(0.11%)	485	(0.23%)
Deaths						
Cardiovascular deaths	245	(0.10%)	29	(0.08%)	216	(0.10%)
Cancer deaths	443	(0.18%)	48	(0.12%)	395	(0.19%)
Deaths: other known cause	153	(0.06%)	17	(0.04%)	136	(0.07%)
Deaths: unknown cause	56	(0.02%)	14	(0.04%)	42	(0.02%)
Deaths: not yet adjudicated	200	(0.08%)	44	(0.11%)	156	(0.08%)
Total death	1097	(0.45%)	152	(0.40%)	945	(0.46%)

[1] Participants with unmarked ethnicity are classified as Minority.
[2] "CHD" includes clinical MI, and coronary death.
[3] "Coronary disease" includes clinical MI, coronary death, angina, congestive heart failure, and CABG/PTCA.
[4] Excludes four cases with borderline malignancy.
[5] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.
[6] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.
[7] Excludes non-melanoma skin cancer
[8] Only women from three bone density clinics.
[9] "Other fracture" excludes fractures indicated as pathological.
[10] Hip fractures are adjudicated at all clinics, while other fractures are adjudicated only at a few clinics. A combined annualized percentage cannot be computed.

Table 5.6 (Continued)
Locally Verified Outcomes (Annualized Percentages) by Age for Observational Study

Data as of: February 29, 2000

Outcome	Age 50-54		55-59		60-69		70-79	
Number enrolled	12388		17321		41216		22796	
Mean follow-up (months)	35.1		33.6		30.2		30.2	
Cardiovascular								
CHD[1]	13	(0.04%)	41	(0.08%)	183	(0.18%)	254	(0.44%)
Coronary death	1	(0.00%)	3	(0.01%)	32	(0.03%)	67	(0.12%)
Clinical MI	12	(0.03%)	38	(0.08%)	157	(0.15%)	210	(0.37%)
Angina	48	(0.13%)	100	(0.21%)	438	(0.42%)	400	(0.70%)
CABG/PTCA	23	(0.06%)	80	(0.16%)	346	(0.33%)	335	(0.58%)
Carotid artery disease	14	(0.04%)	12	(0.02%)	69	(0.07%)	86	(0.15%)
Congestive heart failure	13	(0.04%)	33	(0.07%)	195	(0.19%)	233	(0.41%)
Stroke	8	(0.02%)	33	(0.07%)	145	(0.14%)	205	(0.36%)
PVD	4	(0.01%)	13	(0.03%)	44	(0.04%)	67	(0.12%)
Coronary disease[2]	67	(0.19%)	160	(0.33%)	744	(0.72%)	792	(1.38%)
Total CVD	87	(0.24%)	204	(0.42%)	942	(0.91%)	1063	(1.85%)
Cancer								
Breast cancer[3]	132	(0.36%)	199	(0.41%)	505	(0.49%)	289	(0.50%)
Invasive breast cancer	108	(0.30%)	164	(0.34%)	404	(0.39%)	239	(0.42%)
In situ breast cancer	25	(0.07%)	37	(0.08%)	103	(0.10%)	48	(0.08%)
Ovary cancer	9	(0.02%)	17	(0.04%)	47	(0.05%)	31	(0.05%)
Endometrial Cancer[4]	13	(0.06%)	15	(0.05%)	73	(0.12%)	44	(0.14%)
Colorectal cancer	11	(0.03%)	28	(0.06%)	101	(0.10%)	98	(0.17%)
Other cancer[5,6]	79	(0.22%)	136	(0.28%)	432	(0.42%)	341	(0.59%)
Total cancer	241	(0.67%)	387	(0.80%)	1143	(1.10%)	788	(1.37%)
Fractures								
Hip fracture	3	(0.01%)	22	(0.05%)	64	(0.06%)	117	(0.20%)
Vertebral fracture[7]	1	(0.03%)	3	(0.07%)	11	(0.12%)	22	(0.41%)
Other fracture[5,7,8]	38	(1.17%)	46	(1.10%)	117	(1.22%)	92	(1.70%)
Total fracture[9]	42	(0.12%)	71	(0.15%)	188	(0.18%)	225	(0.39%)
Deaths								
Cardiovascular deaths	5	(0.01%)	13	(0.03%)	81	(0.08%)	146	(0.25%)
Cancer deaths	24	(0.07%)	53	(0.11%)	195	(0.19%)	171	(0.30%)
Deaths: other known cause	8	(0.02%)	19	(0.04%)	61	(0.06%)	65	(0.11%)
Deaths: unknown cause	3	(0.01%)	5	(0.01%)	25	(0.02%)	23	(0.04%)
Deaths: not yet adjudicated	9	(0.02%)	12	(0.02%)	83	(0.08%)	96	(0.17%)
Total death	49	(0.14%)	102	(0.21%)	445	(0.43%)	501	(0.87%)

[1] "CHD" includes clinical MI, and coronary death.
[2] "Coronary disease" includes clinical MI, coronary death, angina, congestive heart failure, and CABG/PTCA.
[3] Excludes four cases with borderline malignancy.
[4] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.
[5] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.
[6] Excludes non-melanoma skin cancer
[7] Only women from three bone density clinics.
[8] "Other fracture" excludes fractures indicated as pathological.
[9] Hip fractures are adjudicated at all clinics, while other fractures are adjudicated only at a few clinics. A combined annualized percentage cannot be computed.

Table 5.7
Counts (Annualized Percentages) of Participants with Self-Reported Outcomes by Ethnicity and Age for Observational Study

Data as of: February 29, 2000

Outcomes	Total		Ethnicity: Minority[1]		Ethnicity: White	
Number enrolled	93721		15697		78024	
Mean follow-up (months)	31.5		29.4		31.9	
Hospitalizations						
Ever	17506	(7.12%)	2297	(5.98%)	15209	(7.34%)
Two or more	5455	(2.22%)	691	(1.80%)	4764	(2.30%)
Other						
DVT[2]	256	(0.10%)	28	(0.07%)	228	(0.11%)
PE	133	(0.05%)	10	(0.03%)	123	(0.06%)
Diabetes (treated)	4070	(1.66%)	1361	(3.54%)	2709	(1.31%)
Gallbladder disease[3]	2552	(1.04%)	365	(0.95%)	2187	(1.06%)
Hysterectomy[4]	1288	(0.89%)	195	(0.97%)	1093	(0.88%)
Glaucoma	3199	(1.30%)	790	(2.06%)	2409	(1.16%)
Osteoporosis	9466	(3.85%)	1182	(3.08%)	8284	(4.00%)
Osteoarthritis[5]	13510	(5.50%)	2319	(6.04%)	11191	(5.40%)
Rheumatoid arthritis	2227	(0.91%)	730	(1.90%)	1497	(0.72%)
Intestinal polyps	4900	(1.99%)	749	(1.95%)	4151	(2.00%)
Lupus	400	(0.16%)	80	(0.21%)	320	(0.15%)
Kidney Stones[5]	705	(0.45%)	151	(0.59%)	554	(0.42%)
Cataracts[5]	12257	(7.77%)	1938	(7.56%)	10319	(7.81%)
Pills for hypertension	24976	(10.17%)	5302	(13.80%)	19674	(9.50%)

Outcome	Age: 50-54		Age: 55-59		Age: 60-69		Age: 70-79	
Number enrolled	12388		17321		41216		22796	
Mean follow-up (months)	35.1		33.6		30.2		30.2	
Hospitalizations								
Ever	1669	(4.61%)	2547	(5.25%)	7631	(7.36%)	5659	(9.87%)
Two or more	458	(1.27%)	684	(1.41%)	2360	(2.28%)	1953	(3.41%)
Other								
DVT[2]	18	(0.05%)	28	(0.06%)	110	(0.11%)	100	(0.17%)
PE	15	(0.04%)	11	(0.02%)	59	(0.06%)	48	(0.08%)
Diabetes (treated)	414	(1.14%)	665	(1.37%)	1880	(1.81%)	1111	(1.94%)
Gallbladder disease[3]	391	(1.08%)	481	(0.99%)	1106	(1.07%)	574	(1.00%)
Hysterectomy[4]	200	(0.93%)	241	(0.80%)	574	(0.95%)	273	(0.85%)
Glaucoma	271	(0.75%)	414	(0.85%)	1430	(1.38%)	1084	(1.89%)
Osteoporosis	788	(2.18%)	1332	(2.75%)	4317	(4.16%)	3029	(5.28%)
Osteoarthritis[5]	1190	(3.29%)	1994	(4.11%)	5945	(5.73%)	4381	(7.64%)
Rheumatoid arthritis	305	(0.84%)	413	(0.85%)	881	(0.85%)	628	(1.10%)
Intestinal polyps	508	(1.40%)	862	(1.78%)	2213	(2.13%)	1317	(2.30%)
Lupus	72	(0.20%)	88	(0.18%)	159	(0.15%)	81	(0.14%)
Kidney Stones[5]	83	(0.39%)	138	(0.46%)	302	(0.44%)	182	(0.48%)
Cataracts[5]	403	(1.90%)	1080	(3.61%)	5929	(8.66%)	4845	(12.68%)
Pills for hypertension	2212	(6.11%)	3817	(7.87%)	11111	(10.71%)	7836	(13.67%)

[1] Participants with unmarked ethnicity are classified as Minority.
[2] Inpatient DVT only.
[3] "Gallbladder disease" includes self-reports of both hospitalized and non-hospitalized events.
[4] Only women without a baseline hysterectomy are used to compute the annual rates of hysterectomy.
[5] These outcomes have not been self-reported on all versions of Form 33. The annualized percentages are corrected for the different amounts of follow-up.

6. Outcomes Processing

6.1 Overview

Most outcomes are initially ascertained by self-report on *Form 33 – Medical History Update*. CT participants complete this form every six months; OS participants complete this form every year. Those participants who report an outcome requiring documentation and adjudication are asked to complete a more detailed form (*Form 33D*) that collects the information needed to request the associated medical records.

After these forms are completed and entered into the database, the CCs execute a database function that identifies adjudication cases based on the *Form 33D* information. CCs then request hospital and related records for each outcome category. Once the cases are documented, clinic staff send the charts for potential cardiovascular, cancer, and fracture outcomes to the local physician adjudicator for evaluation and classification. Upon return, clinic staff enter the local determinations into the WHI database. Key cardiovascular outcomes are further adjudicated by a central committee process. Currently WHI requires central adjudication of all such events. The investigators at UCSF (Steve Cummings, PI) subcontract to the CCC to adjudicate all hip fractures. Staff at the CCC code and adjudicate all cancers of major interest in the study (breast, colon, rectum, ovary, and endometrium) using standardized SEER guidelines. In addition to the cardiovascular, cancer, and fracture outcome data, which are adjudicated, outcomes for selected other diseases, such as diabetes, gallbladder disease, and hysterectomy, are collected as self-reports only.

The monitoring analysis is conducted on outcomes as classified by the local adjudicator. Currently about 91% of the self-reports have been adjudicated. We do *not* report on the self-reports for which the adjudication process is not yet finished. We feel that we have now reached the stage in the study where the fraction of the self-reports that are not yet adjudicated is sufficiently small that omitting unadjudicated self-reports does not distort the larger picture. Central adjudication results, while offering a higher degree of standardization, will eventually be available only on a subsample, and even then only after a lag time of several months. The central adjudication process should therefore be viewed primarily as a quality assurance effort.

6.2 Terminology

When a particular outcome, say MI, is investigated, all participants can be divided into five groups:

1. Those who have no self-report of an MI and have no locally confirmed MI.

2. Those who have a self-report of an MI and a locally confirmed MI. We refer to these participants' cases as *confirmed (with self-report)*.

3. Those who have no self-report of an MI but do have a locally confirmed MI usually as a result of an investigation of a self-report of another outcome. We refer to these participants' cases as *confirmed (without self-report)*.

4. Those who have a self-report of an MI but do not have a locally confirmed MI, and for whom all relevant adjudication cases are closed. We refer to these participants' self-reports as *denied*.

5. Those who have a self-report of an MI, but do not have a locally confirmed MI, while some of the relevant adjudication cases are still open. We refer to these participants' self-reports as *open*.

The *confirmed cases* are the cases of participants in categories 2 and 3; the *self-reports* are the cases of participants in categories 2, 4, and 5; the *closed self-reports* are the cases of participants in categories 2 and 4. For some analyses we divide the *denied* self-reports into three groups:

4a. The reports of the participants for which the self-reported outcome was denied, but for whom a related outcome (e.g., an angina based on an MI self-report) was found. We refer to those participants' self-reports as *denied - related outcome found*. For the outcome tables, we consider all cardiovascular outcomes to be related, all cancer outcomes to be related, and all fracture outcomes to be related.

4b. The reports of the participants for which the self-reported outcome was denied after review of the relevant documentation. We refer to those participants' self-reports as *denied - no (related) outcome found*.

4c. The reports of the participants for which the self-report was *denied* for *administrative reasons*. Self-reports can only be denied if they satisfy one of several narrowly defined rules. Usually this means that no documentation was obtained after several attempts over a one-year period. Reasons for not obtaining documentation are:

- The provider named by the participant does not have or will not release documentation about the WHI participant, and the WHI participant is not able to name another provider

- The provider indicated by the participant does not respond after repeated contacts by the CC over a period of at least one year (common for hospitalizations out of the country).

6.3 Outcomes Data Quality

Tables 6.1-6.2 – Timeliness and Completeness of Local Adjudications displays the distribution of time required to locally adjudicate a self-reported outcome by month of *Form 33*, for the CT and the OS, respectively. This table is based on the day on which the form was received by the clinic, which may not be the same as the day on which the form was entered in the database. Thus, some of the more recent data will improve when more adjudications are key entered. Overall 91% of self-reported outcomes in the CT and 90% of the self-reported outcomes in the OS requiring adjudication have been closed. In particular, 45% of the outcomes in the CT and 49% of the outcomes in the OS have been closed within 90 days of self-report and 65% (CT) and 71% (OS) within 180 days. (Note: the fact that the percentages for the OS appear better is because most of the outcomes in 1996 and earlier, when outcomes processing was considerably slower, are CT outcomes.)

Since the May 1998 DSMB meeting, there has been a coordinated effort from CCs, CCC, Project Office, Performance Monitoring Committee, and Outcomes Efficiency Task Force to improve the timeliness and completeness of the local adjudication process. The percentage of forms that were adjudicated within 90 days has increased from about 40% to about 65%, and the percentage of forms that were adjudicated within 180 days has increased from about 60% to about 85%. At the same time, the percentage of forms that are more than a year old that have not yet been adjudicated has been reduced to 1.8% for the CT and 2.5% for the OS. Currently 24 of the 40 clinics have ten or fewer outstanding *Forms 33D* that are more than a year.

Figures 6.1-6.2 – Timeliness of Adjudications display Kaplan-Meier curves for the time period from reporting an outcome on *Form 33D* until the adjudication case is closed per year of self-report and, for recent data, per quarter of self-report, separately for the CT and OS. Both figures clearly show that improvements in the processing of outcomes have happened throughout the study.

The outcomes ascertainment, documentation and adjudication effort is by necessity a lengthy process involving interaction between the clinical center, the participant, and her health care providers. Some of the biggest hurdles are related to the interactions with the providers, and these will continue to slow the outcomes process, particularly when the event of interest occurred near the time of the participant's self-report. In these instances the chart may not be complete or available, causing CCs to issue multiple requests. The CCC continues to work closely with the Outcomes Performance Monitoring Committee (OPMC) to develop reports and other tools that will facilitate timely outcomes processing by the CCs.

Tables 6.3-6.4 – Agreement of Local Adjudications with Self-Reports shows condition types that the participant can indicate on *Form 33* or *Form 33D* and the fraction of time that the local adjudicator agrees with that self-report. Because of the complications of the adjudication process, it is not straightforward to define an appropriate estimate of the accuracy of individual self-reports. For example, for most outcome types second occurrences do not need to be adjudicated, but if the participant reports a second occurrence before the first is confirmed, an adjudication case will be opened anyway. This case will be closed without a locally confirmed outcome when the first self-report is confirmed. To circumvent this and similar problems, the unit in *Tables 6.3* and *6.4* is defined to be a *participant* rather than an outcome event. For some participants whose self-report is denied, related outcomes may be found. We also note that on *Form 33* and *Form 33D* participants report a "stroke or transient ischemic attack (TIA)," while for monitoring purposes only the outcome "stroke" is used. Thus, the number of confirmed cases in *Table 6.3* and *6.4*, which include TIA, is substantially larger than that in some of the outcomes tables.

A self-reported outcome may be denied for the following reasons: (i) the outcome did take place, but could not be verified because insufficient evidence was available to the WHI adjudicator; (ii) the outcome did not take place, but a related outcome (which may or may not be of interest to WHI) occurred; (iii) the outcome took place before enrollment in WHI; and (iv) the current self-report was a duplicate report of a previous self-report.

The accuracy of self-reports varies considerably by outcome. For many outcomes the agreement rates for the CT are a few percentage points higher than for the OS. The accuracy of

cancer and fracture self-reports may be higher than that for cardiovascular disease because more cardiovascular self-reports result in a related outcome. If those related outcomes are included with the confirmed self-reports, cardiovascular outcomes have a 79% agreement rate between self-reports and locally confirmed outcomes (88% if we exclude angina, which is probably the softest cardiovascular outcome), cancer outcomes have an agreement rate of 86% (91% for the primary cancers), and fracture outcomes have an agreement rate of 79% for the CT and OS combined.

Note that the accuracy of self-reports for *other fractures* (*other cancers*) reflects the percentage of people who reported an *other fracture* (*other cancer*) for whom any of the fractures (cancers) in the other category was found, even if the participant indicated the wrong skeletal site (cancer site).

Tables 6.5-6.6 – Agreement of Central Adjudications with Local Adjudications shows that there is good agreement between local and central adjudications for all outcomes. Often angina and congestive heart failure occur in conjunction with an MI. Disagreement on angina or CHF, when there is agreement about the MI, is not considered very serious. Some self-reports are locally adjudicated as one type of outcome, while they are centrally adjudicated as another outcome. Since we see the central adjudication process primarily as quality assurance, data regarding such cross-classification is not shown.

There is a considerable backlog of locally confirmed cases that have not yet been centrally adjudicated. This backlog is partly artificial, as it takes about three-four months for a locally confirmed case to finish the central adjudication process. The CCC cancer coders are currently making it a top-priority to reduce the backlog for cancer cases; in fact, the backlog for ovary, endometrial, and colorectal cancer has already been reduced substantially since the previous report.

6.4 Outcomes Data Summary

Table 6.7 – Locally Verified Outcomes (Annualized Percentages) by Ethnicity and by Age for CT contains the number of locally verified outcomes for the major WHI outcomes. Since a number of the outcomes still need to be adjudicated, the numbers in these tables give a lower bound on the number of outcomes that currently have occurred. We estimate that the actual number of cases for most outcomes is currently about 10-15% larger than what is reported here. When we get further in the study the number of not yet adjudicated cases will decrease as a fraction if the total number of cases.

Currently, for the CT we observe approximately 80% of the invasive breast and colorectal cancer cases of what was assumed for the power calculations. The observed rate of CHD is approximately 80% of what was assumed for the 55-59 and 60-69 age categories. The rate in the youngest age category, 50-54 at baseline, is actually slightly higher than what was assumed. Only in the oldest age category, 70-79 at baseline, are the current observed rates considerably lower (about 50%) than design assumptions. The participants in the oldest age category were among the latest to be recruited, so the "healthy volunteer effect" may still be an important factor for these women. When we combine the four age categories, the observed rate is about

70% of what was assumed in the design. The rates of hip fractures are currently only about 30% of what was assumed for all age categories.

Table 6.8 – Counts (Annualized Percentages) of Participants with Self-Reported Outcomes by Ethnicity and Age for CT contain counts of the number of self-reports for some of the WHI outcomes that are not verified. As for many of the confirmed outcomes, the participants over report (see *Tables 6.3-6.4).* The numbers in these tables should be seen as upper bounds to the number of outcomes that has currently occurred. Not surprisingly, for many of the outcomes the rates differ considerably by minority status and by age at baseline.

Similar tables for the HRT, DM, CaD and the OS components are in the chapters about these components. Currently, the rates of cancer and fractures in the OS and CT are very similar. The rate of cardiovascular events is somewhat higher in the CT than in the OS. One possible explanation is that the eligibility criteria for the DM, which excluded women who were eating a low percentage of fat from calories, may have moved a group at lower risk of cardiovascular disease from the CT to the OS.

Tables 6.9 – Other Cancers and *6.10 – Other Fractures* split out the other cancers and other fractures for the locally verified outcomes by event type and by study. Since for OS participants other fractures are only locally verified at the three bone mineral density clinics, we provide the number of self-reported fractures for these participants.

6.5 ECG Data

Electrocardiograms (ECGs) are given to all CT participants at baseline, and years 3, 6 and 9. The ECGs are sent to EPICARE (Pentti Rauthaharju, PI), which subcontracts to the CCC. EPICARE provides the CCC with a comprehensive analysis of each individual ECG, as well as with a serial analysis of the follow-up ECGs of a participant relative to that participant's baseline ECG. This serial analysis is intended to identify silent MIs: MIs that are detected by this ECG analysis, but were not reported by the participant. Analysis of individual ECGs may also be of interest since abnormalities in ECGs are known to be predictors of future cardiovascular problems. As of February 29, 2000, the CCC has received serial analysis on 31,048 CT participants whose year 3 ECGs have been analyzed by EPICARE.

Table 6.11 – Cross-tabulation of ECG Codes and Locally Confirmed MI for All CT Participants shows the relation between MIs that have been identified prior to the year 3 ECG and incident MIs as identified by the ECG analysis. Since the previous DSMB report, Dr. Rauthaharju has carried out an additional level of quality control on the ECGs. As a result of this quality control, the number of (possible) evolving Q-wave MIs has been reduced since the last report. A total of 25 evolving Q-wave MIs have been identified. We note that 11 of these MIs were also identified by the regular outcomes reporting process. The remaining 14 evolving Q-wave MIs are thus the "definite silent MIs." *Table 6.11* also gives the number of possible silent MIs.

6.6 Vital Status

Table 6.12 – Cause of Death presents the cause of death for CT and OS participants. To reduce the time that it takes before cause of death information is available on WHI participants who have passed away, death adjudication procedures were changed in April 1999 to encourage clinics to report a "temporary" cause of death for those participants for whom some, but not all, documentation related to the death has been collected. This change in procedures was made in recognition of the fact that it is often more difficult to obtain documents for death cases than for self-reports, for which participants can sign a release themselves. The goal is that a temporary cause is entered in the database as soon as possible, preferably within eight weeks. The cause based on the complete documentation should be entered as soon as all documents are collected. Cases for which reported unsuccessful requests for documentation have been made over a one year period can be closed out with incomplete documentation. This happens, for example, when deaths occur outside the country, or when the death resulted in litigation.

As of the February 29, 2000 database, there were 773 deaths in the CT and 1097 in the OS. Of the 773 CT deaths, there were 633 (80%) for which a final adjudication was available, and an additional 33 (4%) for which a temporary adjudication was available. These 773 CT deaths include 27 that were first reported between January 1 and February 29 of this year. Of the 746 that were first reported before January 1, 2000, 614 have a final adjudication and 29 have a temporary one, giving us cause of death information on 86% of the CT deaths. For the OS there is cause of death information on 82% of all deaths, and 84% of all deaths that were reported before January 1, 2000. Unfortunately, the percentage of deaths that are more than two months old, for which cause of death information is available, has dropped slightly in the last six months.

Table 6.13 – Lost-to-Follow-up and Vital Status by Clinic: CT Participants displays information about the follow-up and vital status by clinic. Since June 1999, clinics are regularly provided with a list of participants for whom there is no *Form 33* within the last 18 months and who are not known to be deceased. Clinics are asked to make every effort to try to locate these participants and to encourage further study participation. Some participants had information in the database that indicated that she never wanted to be contacted again by WHI. If this were the case, clinics were to verify whether this participation status was correct. If indeed a participant has expressed this opinion, she is not to be contacted again. For these participants, we will still be able to obtain limited vital status information when WHI will carry out a National Death Index (NDI) search. (The first NDI search is planned for later this year.)

About 1.1% of the CT participants are deceased, we do not know the vital status of about 1.5% of the CT participants, and 1.2% of the participants request no further follow-up. In addition, we lack recent outcomes information on an additional 0.1% of the participants. The study design assumed that 3% per year of the participants would be lost-to-follow-up or death. As the average follow-up of participants is now 3.2 years, we note that the follow-up is much better than what was assumed in the design.

There is considerable clinic-to-clinic variation in the vital status data. The percentage of participants with unknown vital status ranges from 0.1 to 7.2% per clinic. The percentage of participants who stopped follow-up ranges from less than 0.1 to 5.1%.

Table 6.14 – Lost-to-Follow-up and Vital Status by Clinic: OS contains the same information as *Table 6.13* about the OS. For OS, the participants are considered lost-to-follow-up if we have not received a *Form 33* within the last 24 months. Approximately 2.5% of the OS participants is either lost-to-follow-up or has stopped follow-up. While these numbers appear better than those for the CT, we should keep in mind that OS participants have six months more before they are considered lost-to-follow-up, and OS participants have, on the average, been recruited more recently than CT participants. In addition, some OS participants have been in the study for fewer than 24 months. Those participants would be classified as "current participation" or "recent participation," even if they never filed a *Form 33*.

Table 6.1
Timeliness and Completeness of Local Adjudications - CT[1]

Data as of: February 29, 2000

Forms with conditions[2]		Number and % of forms with conditions locally adjudicated by days from Form 33 encounter date to completion of local adjudication							
Date of Form 33 encounter		≤ 90		≤ 180		Closed		Open	
	N	N	%	N	%	N	%	N	%
<= June 30 1996	3911	266	7	775	20	3864	99	47	1
1996 July - December	1380	309	22	723	52	1363	99	17	1
1997 January-June	2169	765	35	1336	62	2153	99	16	1
1997 July-December	2532	976	39	1515	60	2506	99	26	1
1998 January-June	3572	1669	47	2793	78	3526	99	46	1
1998 July-December	4147	2372	57	3354	81	4038	97	109	3
1999 January	736	450	61	626	85	703	96	33	4
1999 February	695	421	61	568	82	654	94	41	6
1999 March	815	506	62	682	84	768	94	47	6
1999 April	769	484	63	662	86	724	94	45	6
1999 May	760	496	65	648	85	701	92	59	8
1999 June	799	504	63	674	84	719	90	80	10
1999 July	724	488	67	618	85	637	88	87	12
1999 August	759	486	64	647	85	666	88	93	12
1999 September	716	472	66	602	84			114	16
1999 October	768	490	64	608	79			160	21
1999 November	737	486	66	538	73			199	27
1999 December	702	482	69					220	31
2000 January	750	303	40					447	60
2000 February	540	45	8					495	92
Total	27981	12470	45	18199	65	25600	91	2381	9

[1] This table is based on the day *Form 33* was received by the clinic, not on the day the form was entered in the database.

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

Table 6.2
Timeliness and Completeness of Local Adjudications - OS[1]

Data as of: February 29, 2000

Forms with conditions[2]		Number and % of forms with conditions locally adjudicated by days from Form 33 encounter date to completion of local adjudication							
Date of Form 33 encounter		≤ 90		≤ 180		Closed		Open	
	N	N	%	N	%	N	%	N	%
<= June 30 1996	236	86	36	129	55	234	99	2	1
1996 July - December	1308	311	24	709	54	1295	99	13	1
1997 January-June	2150	851	40	1411	66	2115	98	35	2
1997 July-December	2292	715	31	1370	60	2252	98	40	2
1998 January-June	2827	1279	45	2057	73	2772	98	55	2
1998 July-December	3784	2019	53	2929	77	3645	96	139	4
1999 January	643	367	57	545	85	616	96	27	4
1999 February	734	448	61	630	86	699	95	35	5
1999 March	854	506	59	686	80	799	94	55	6
1999 April	823	521	63	710	86	780	95	43	5
1999 May	774	482	62	662	86	720	93	54	7
1999 June	913	580	64	785	86	843	92	70	8
1999 July	718	440	61	610	85	642	89	76	11
1999 August	810	523	65	694	86	708	87	102	13
1999 September	759	473	62	638	84			121	16
1999 October	680	401	59	532	78			148	22
1999 November	700	438	63	495	71			205	29
1999 December	512	313	61					199	39
2000 January	648	254	39					394	61
2000 February	561	61	11					500	89
Total	22726	11068	49	16220	71	20413	90	2313	10

[1] This table is based on the day *Form 33* was received by the clinic, not on the day the form was entered in the database.

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

Figure 6.1 Clinical Trial Timeliness per Period of Self-Report

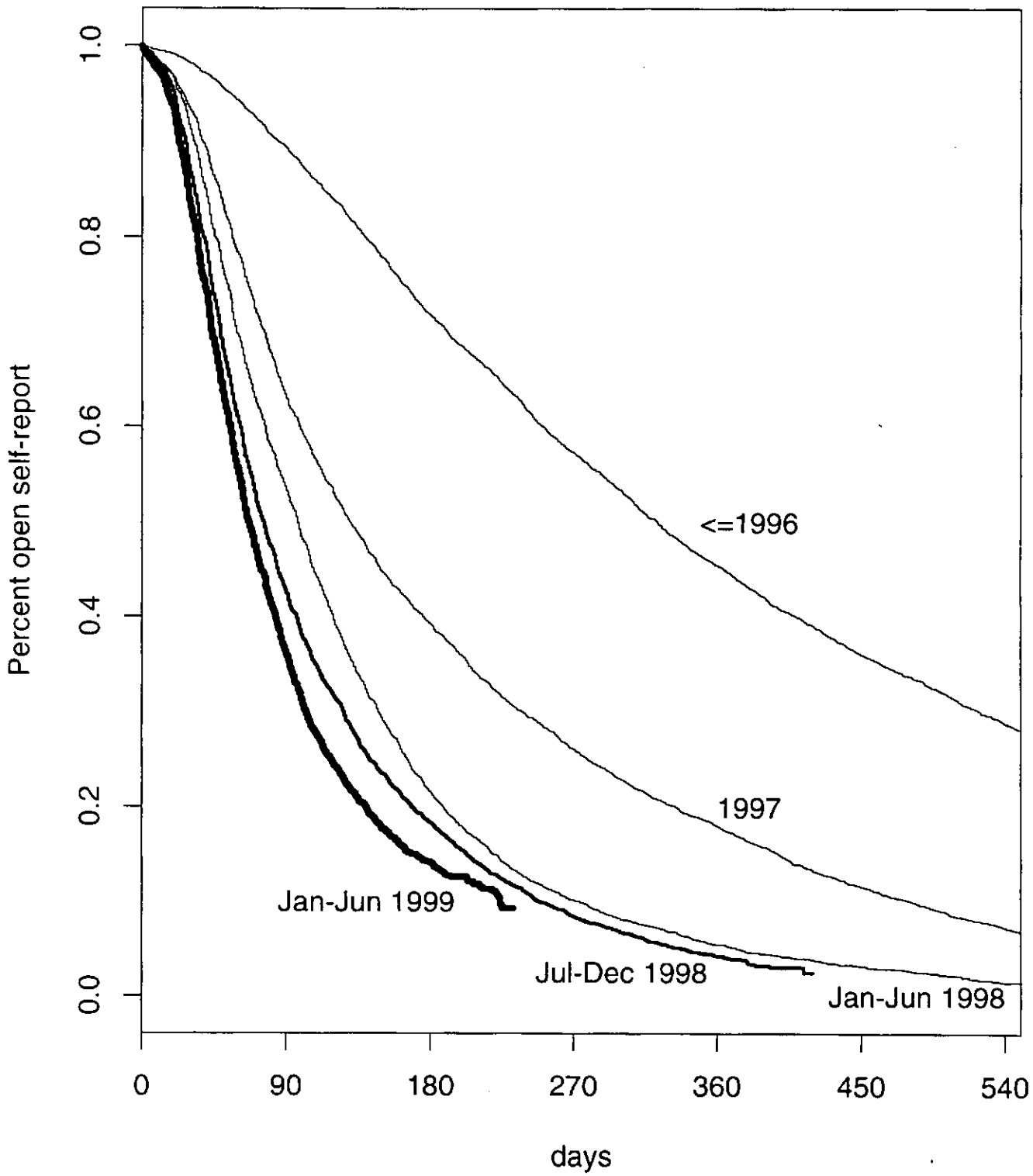


Figure 6.2 Observational Study Timeliness per Period of Self-Report

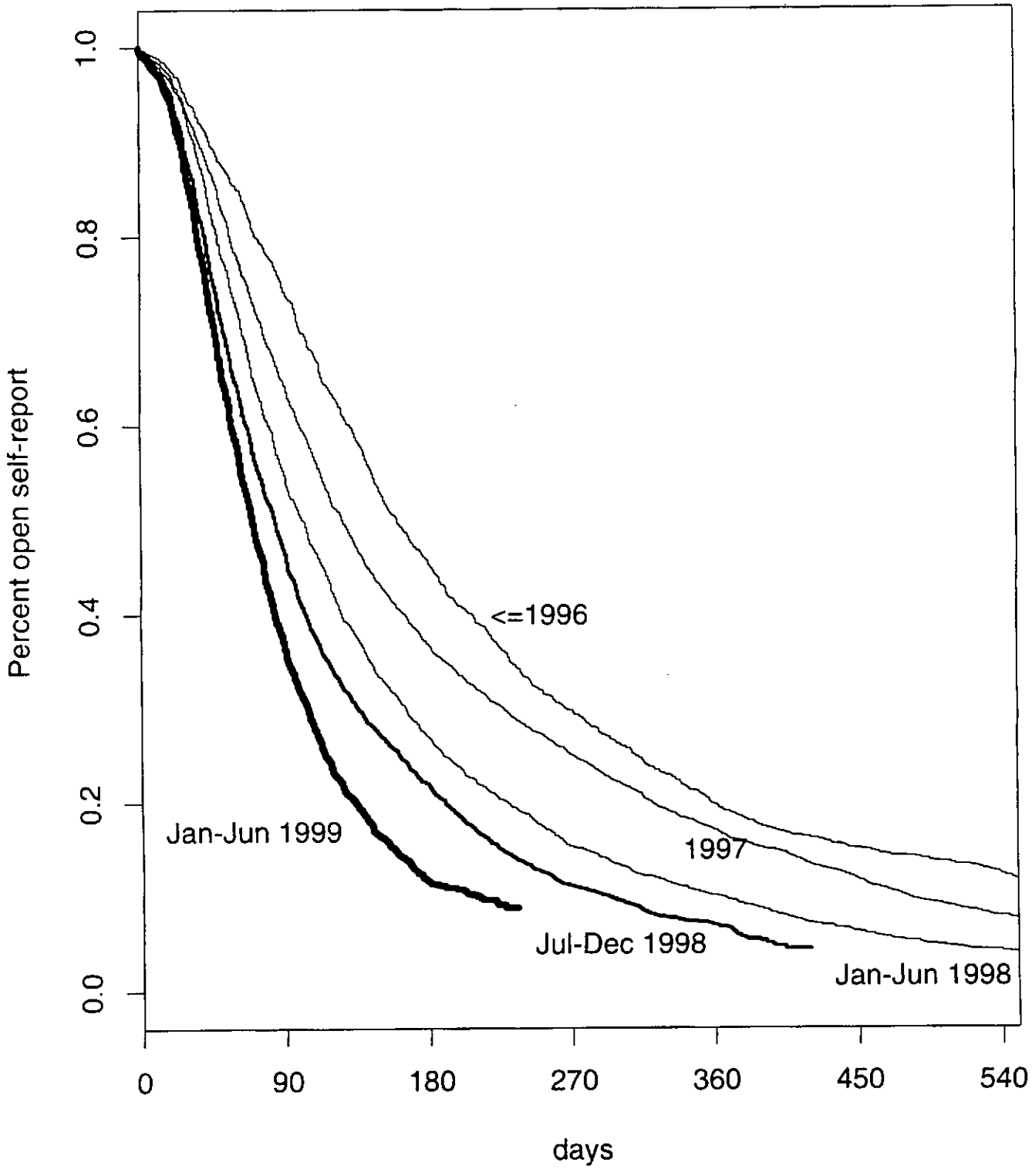


Table 6.3
Agreement of the Local Adjudications with Self-Reports — CT

Data as of: February 29, 2000

	Participants with a self-report	Closed		Confirmed		Denied – related outcome found		Denied – no outcome found		Administrative denials	
		N	%	N	%[1]	N	%[1]	N	%[1]	N	%[1]
Cardiovascular											
MI	510	465	91%	338	(73%)	66	(14%)	55	(12%)	6	(1%)
Angina[2]	1163	1030	89%	425	(41%)	166	(16%)	418	(41%)	21	(2%)
Congestive heart failure	306	262	86%	184	(70%)	21	(8%)	52	(20%)	5	(2%)
CABG/PTCA	911	804	88%	707	(88%)	60	(7%)	30	(4%)	7	(1%)
Carotid artery disease[3]	158	138	87%	112	(81%)	17	(12%)	8	(6%)	1	(1%)
Stroke/TIA[4]	759	670	88%	522	(78%)	33	(5%)	105	(16%)	10	(1%)
PVD	104	91	88%	57	(63%)	11	(12%)	21	(23%)	2	(2%)
DVT[5]	174	151	87%	105	(70%)	22	(15%)	20	(13%)	4	(3%)
PE[5]	74	67	91%	59	(88%)	3	(4%)	5	(7%)	0	(0%)
Cancers											
Breast cancer	960	841	88%	802[6]	(95%)	1	(0%)	36	(4%)	2	(0%)
Ovary cancer	105	98	93%	72	(73%)	21	(21%)	3	(3%)	2	(2%)
Endometrial cancer	137	122	89%	84	(69%)	23	(19%)	14	(11%)	1	(1%)
Colorectal	288	252	88%	221	(88%)	15	(6%)	14	(6%)	2	(1%)
Other cancer[7]	1133	989	87%	737	(75%)	60	(6%)	169	(17%)	23	(2%)
Fractures											
Hip fracture	196	165	84%	135	(82%)	6	(4%)	21	(13%)	3	(2%)
Vertebral fracture	360	312	87%	161	(52%)	10	(3%)	127	(41%)	14	(4%)
Other fracture	3673	3339	91%	2692	(81%)	22	(1%)	533	(16%)	92	(3%)

[1] Percentages between parentheses are relative to "closed."

[2] Angina that is self-reported after a confirmed MI, is not adjudicated. In particular, 119 self-reports of angina (115 denied related, 3 denied, 1 administrative denial) are associated with participants who have a confirmed MI

[3] Carotid artery disease that is self-reported after a confirmed Stroke, is not adjudicated. In particular, 2 self-reports of Carotid artery disease (2 denied related) are associated with participants who have a confirmed Stroke.

[4] Stroke and TIA have a combined self-report. Only stroke is monitored. There were 152 participants who reported stroke/TIA for whom only TIA was confirmed.

[5] HRT Participants only

[6] There were 610 confirmed cases of invasive breast cancer and 194 confirmed cases of in situ breast cancer.

[7] Excludes non-melanoma skin cancer

Table 6.4
Agreement of the Local Adjudications with Self-Reports — OS

Data as of: February 29, 2000

	Participants with a self-report	Closed		Confirmed		Denied – related outcome found		Denied – no outcome found		Administrative denials	
		N	%	N	%[1]	N	%[1]	N	%[1]	N	%[1]
Cardiovascular											
MI	419	334	80%	218	(65%)	70	(21%)	43	(13%)	3	(1%)
Angina[2]	1205	1051	87%	455	(43%)	115	(11%)	458	(44%)	23	(2%)
Congestive heart failure	326	284	87%	195	(69%)	19	(7%)	64	(23%)	6	(2%)
CABG/PTCA	959	816	85%	686	(84%)	66	(8%)	54	(7%)	10	(1%)
Carotid artery disease[3]	183	160	87%	121	(76%)	24	(15%)	13	(8%)	2	(1%)
Stroke/TIA[4]	811	676	83%	506	(75%)	27	(4%)	126	(19%)	17	(3%)
PVD	140	115	82%	66	(57%)	14	(12%)	32	(28%)	3	(3%)
Cancers											
Breast cancer	1383	1173	85%	1051[5]	(90%)	5	(0%)	106	(9%)	11	(1%)
Ovary cancer	121	109	90%	71	(65%)	15	(14%)	21	(19%)	2	(2%)
Endometrial cancer	139	123	88%	90	(73%)	20	(16%)	11	(9%)	2	(2%)
Colorectal	279	239	86%	197	(82%)	16	(7%)	21	(9%)	5	(2%)
Other cancer[6]	1399	1171	84%	788	(67%)	94	(8%)	249	(21%)	40	(3%)
Fractures											
Hip fracture	259	216	83%	169	(78%)	7	(3%)	32	(15%)	8	(4%)
Vertebral fracture	52	47	90%	28	(60%)	6	(13%)	10	(21%)	3	(6%)
Other fracture	394	355	90%	270	(76%)	7	(2%)	68	(19%)	10	(3%)

[1] Percentages between parentheses are relative to "closed."

[2] Angina that is self-reported after a confirmed MI, is not adjudicated. In particular, 62 self-reports of angina (60 denied related, 2 denied) are associated with participants who have a confirmed MI

[3] Carotid artery disease that is self-reported after a confirmed Stroke, is not adjudicated. In particular, 3 self-reports of Carotid artery disease (3 denied related) are associated with participants who have a confirmed Stroke.

[4] Stroke and TIA have a combined self-report. Only stroke is monitored. There were 179 participants who reported stroke/TIA for whom only TIA was confirmed.

[5] There were 855 confirmed cases of invasive breast cancer and 201 confirmed cases of in situ breast cancer.

[6] Excludes non-melanoma skin cancer

Table 6.5
Agreement of Central Adjudications with Local Adjudications — CT

Data as of: February 29, 2000

	Locally confirmed N	Centrally adjudicated N	%	In agreement N	%[1]
Cardiovascular					
MI	497	315	63%	275	87%
Angina[2]	874	639	73%	498	78%
Congestive heart failure	392	267	68%	199	75%
CABG/PTCA	772	543	70%	525	97%
DVT[3]	128	80	63%	74	93%
PE[3]	76	47	62%	44	94%
Cancers					
Breast cancer	823	283	34%	279	99%
Invasive	620	211	34%	205	97%
Non Invasive	196	68	35%	52	76%
Ovary cancer	88	64	73%	54	84%
Endometrial cancer	109	83	76%	79	95%
Colorectal cancer	243	172	71%	169	98%
Fractures					
Hip fracture	124	74	60%	70	95%

[1] Percentage is relative to centrally adjudicated cases

[2] Participants with a confirmed MI no longer require adjudication of angina

[3] HRT only; DVT and PE are centrally adjudicated since May of 1997

Table 6.6
Agreement of Central Adjudications with Local Adjudications — OS

Data as of: February 29, 2000

	Locally confirmed N	Centrally adjudicated N	Centrally adjudicated %	In agreement N	In agreement %[1]
Cardiovascular					
MI	417	259	62%	215	83%
Angina[2]	943	649	69%	534	82%
Congestive heart failure	474	304	64%	248	82%
CABG/PTCA	784	518	66%	497	96%
Cancers					
Breast cancer	1089	342	31%	328	96%
Invasive	879	252	29%	246	98%
Non Invasive	210	76	36%	57	75%
Ovary cancer	95	68	72%	51	75%
Endometrial cancer	138	107	78%	97	91%
Colorectal cancer	221	145	66%	134	92%
Fractures					
Hip fracture	206	147	71%	143	97%

[1] Percentage is relative to centrally adjudicated cases

[2] Participants with a confirmed MI no longer require adjudication of angina

Table 6.7
Locally Verified Outcomes (Annualized Percentages) by Ethnicity for Clinical Trial

Data as of: February 29, 2000

Outcomes	Total		Minority[1]		White	
Number randomized	68135		12611		55524	
Mean follow-up (months)	38.3		36.5		38.7	
Cardiovascular						
CHD[2]	656	(0.30%)	92	(0.24%)	564	(0.32%)
Coronary death	180	(0.08%)	32	(0.08%)	148	(0.08%)
Total MI[3]	511	(0.24%)	68	(0.18%)	443	(0.25%)
Clinical MI	497	(0.23%)	63	(0.16%)	434	(0.24%)
Definite Silent MI	25	(0.01%)	6	(0.02%)	19	(0.01%)
Possible Silent MI	84	(0.04%)	16	(0.04%)	68	(0.04%)
Angina	916	(0.42%)	156	(0.41%)	760	(0.42%)
CABG/PTCA	772	(0.36%)	97	(0.25%)	675	(0.38%)
Carotid artery disease	169	(0.08%)	19	(0.05%)	150	(0.08%)
Congestive heart failure	392	(0.18%)	69	(0.18%)	323	(0.18%)
Stroke	427	(0.20%)	80	(0.21%)	347	(0.19%)
PVD	113	(0.05%)	24	(0.06%)	89	(0.05%)
CHD[2]/Possible Silent MI	728	(0.34%)	107	(0.28%)	621	(0.35%)
Coronary disease[4]	1826	(0.84%)	299	(0.78%)	1527	(0.85%)
Total CVD	1615	(1.02%)	259	(0.93%)	1356	(1.04%)
Cancer						
Breast cancer[5]	816	(0.38%)	90	(0.23%)	726	(0.41%)
Invasive breast cancer	620	(0.29%)	69	(0.18%)	551	(0.31%)
In situ breast cancer	199	(0.09%)	21	(0.05%)	178	(0.10%)
Ovary cancer	92	(0.04%)	11	(0.03%)	81	(0.05%)
Endometrial Cancer[6]	109	(0.09%)	14	(0.07%)	95	(0.09%)
Colorectal cancer	247	(0.11%)	47	(0.12%)	200	(0.11%)
Other cancer[7,8]	877	(0.40%)	102	(0.27%)	775	(0.43%)
Total cancer	2104	(0.97%)	260	(0.68%)	1844	(1.03%)
Fractures						
Hip fracture	164	(0.08%)	9	(0.02%)	155	(0.09%)
Vertebral fracture	199	(0.09%)	10	(0.03%)	189	(0.11%)
Other fracture[7,9]	2829	(1.30%)	291	(0.76%)	2538	(1.42%)
Total fracture	3117	(1.44%)	306	(0.80%)	2811	(1.57%)
Deaths						
Cardiovascular deaths	229	(0.11%)	37	(0.10%)	192	(0.11%)
Cancer deaths	299	(0.14%)	38	(0.10%)	261	(0.15%)
Deaths: other known cause	87	(0.04%)	13	(0.03%)	74	(0.04%)
Deaths: unknown cause	33	(0.02%)	7	(0.02%)	26	(0.01%)
Deaths: not yet adjudicated	125	(0.06%)	31	(0.08%)	94	(0.05%)
Total death	773	(0.36%)	126	(0.33%)	647	(0.36%)

1 Participants with unmarked ethnicity are classified as Minority.

2 "CHD" includes clinical MI, definite silent MI and coronary death.

3 "Total MI" includes clinical MI and definite silent MI.

4 "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

5 Excludes seven cases with borderline malignancy.

6 Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

7 Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

8 Excludes non-melanoma skin cancer

9 "Other fracture" excludes fractures indicated as pathological.

Table 6.7 (Continued)
Locally Verified Outcomes (Annualized Percentages) by Age for Clinical Trial

Data as of: February 29, 2000

Outcome	50-54		55-59		60-69		70-79	
Number randomized	9191		14664		31390		12890	
Mean follow-up (months)	44.5		40.6		36.4		35.7	
Cardiovascular								
CHD[1]	45	(0.13%)	67	(0.14%)	314	(0.33%)	230	(0.60%)
Coronary death	9	(0.03%)	13	(0.03%)	90	(0.09%)	68	(0.18%)
Total MI[2]	37	(0.11%)	56	(0.11%)	241	(0.25%)	177	(0.46%)
Clinical MI	34	(0.10%)	56	(0.11%)	232	(0.24%)	175	(0.46%)
Definite Silent MI	5	(0.01%)	2	(0.00%)	13	(0.01%)	5	(0.01%)
Possible Silent MI	10	(0.03%)	14	(0.03%)	32	(0.03%)	28	(0.07%)
Angina	51	(0.15%)	123	(0.25%)	453	(0.48%)	289	(0.75%)
CABG/PTCA	40	(0.12%)	99	(0.20%)	379	(0.40%)	254	(0.66%)
Carotid artery disease	5	(0.01%)	20	(0.04%)	75	(0.08%)	69	(0.18%)
Congestive heart failure	17	(0.05%)	41	(0.08%)	175	(0.18%)	159	(0.41%)
Stroke	16	(0.05%)	36	(0.07%)	201	(0.21%)	174	(0.45%)
PVD	5	(0.01%)	11	(0.02%)	53	(0.06%)	44	(0.11%)
CHD[1]/Possible Silent MI	55	(0.16%)	77	(0.16%)	341	(0.36%)	255	(0.67%)
Coronary disease[3]	108	(0.32%)	213	(0.43%)	877	(0.92%)	628	(1.64%)
Total CVD	96	(0.37%)	181	(0.48%)	798	(1.14%)	540	(2.18%)
Cancer								
Breast cancer[4]	95	(0.28%)	173	(0.35%)	387	(0.41%)	161	(0.42%)
Invasive breast cancer	63	(0.19%)	136	(0.27%)	298	(0.31%)	123	(0.32%)
In situ breast cancer	32	(0.09%)	37	(0.07%)	92	(0.10%)	38	(0.10%)
Ovary cancer	10	(0.03%)	18	(0.04%)	43	(0.05%)	21	(0.05%)
Endometrial Cancer[5]	14	(0.07%)	24	(0.08%)	44	(0.08%)	27	(0.13%)
Colorectal cancer	13	(0.04%)	38	(0.08%)	124	(0.13%)	72	(0.19%)
Other cancer[6,7]	79	(0.23%)	131	(0.26%)	427	(0.45%)	240	(0.63%)
Total cancer	207	(0.61%)	372	(0.75%)	1009	(1.06%)	516	(1.35%)
Fractures								
Hip fracture	8	(0.02%)	10	(0.02%)	54	(0.06%)	92	(0.24%)
Vertebral fracture	8	(0.02%)	19	(0.04%)	88	(0.09%)	84	(0.22%)
Other fracture[6,8]	355	(1.04%)	519	(1.05%)	1321	(1.39%)	634	(1.65%)
Total fracture	366	(1.07%)	541	(1.09%)	1436	(1.51%)	774	(2.02%)
Deaths								
Cardiovascular deaths	9	(0.03%)	16	(0.03%)	107	(0.11%)	97	(0.25%)
Cancer deaths	19	(0.06%)	36	(0.07%)	145	(0.15%)	99	(0.26%)
Deaths: other known cause	7	(0.02%)	14	(0.03%)	38	(0.04%)	28	(0.07%)
Deaths: unknown cause	3	(0.01%)	4	(0.01%)	16	(0.02%)	10	(0.03%)
Deaths: not yet adjudicated	11	(0.03%)	7	(0.01%)	62	(0.07%)	45	(0.12%)
Total death	49	(0.14%)	77	(0.16%)	368	(0.39%)	279	(0.73%)

[1] "CHD" includes clinical MI, definite silent MI, and coronary death.

[2] "Total MI" includes clinical MI and definite silent MI.

[3] "Coronary disease" includes clinical MI, definite silent MI, possible silent MI, coronary death, angina, congestive heart failure, and CABG/PTCA.

[4] Excludes seven cases with borderline malignancy.

[5] Only women without a baseline hysterectomy are used to compute the annual rates of endometrial cancer.

[6] Only one report of "other cancer" or "other fracture" is counted per woman; however, the first other cancer or other fracture of each type is adjudicated.

[7] Excludes non-melanoma skin cancer

[8] "Other fracture" excludes fractures indicated as pathological.

Table 6.8
Counts (Annualized Percentages) of Participants with Self-Reported Outcomes by Ethnicity and Age for Clinical Trial

Data as of: February 29, 2000

Outcomes	Total		Ethnicity: Minority[1]		White	
Number randomized	68135		12611		55524	
Mean follow-up (months)	38.3		36.5		38.7	
Hospitalizations						
Ever	16407	(7.55%)	2664	(6.95%)	13743	(7.68%)
Two or more	5981	(2.75%)	932	(2.43%)	5049	(2.82%)
Other						
DVT[2]	366	(0.17%)	46	(0.12%)	320	(0.18%)
PE	163	(0.08%)	19	(0.05%)	144	(0.08%)
Diabetes (treated)	4153	(1.91%)	1507	(3.93%)	2646	(1.48%)
Gallbladder disease[3]	2621	(1.21%)	440	(1.15%)	2181	(1.22%)
Hysterectomy[4]	961	(0.76%)	125	(0.66%)	836	(0.78%)
Glaucoma	3197	(1.47%)	799	(2.08%)	2398	(1.34%)
Osteoporosis	6389	(2.94%)	848	(2.21%)	5541	(3.10%)
Osteoarthritis[5]	10317	(5.15%)	2118	(5.89%)	8199	(4.98%)
Rheumatoid arthritis	2159	(0.99%)	738	(1.92%)	1421	(0.79%)
Intestinal polyps	4178	(1.92%)	725	(1.89%)	3453	(1.93%)
Lupus	364	(0.17%)	77	(0.20%)	287	(0.16%)
Kidney Stones[5]	769	(0.52%)	157	(0.60%)	612	(0.50%)
Cataracts[5]	10085	(6.83%)	1789	(6.85%)	8296	(6.82%)
Pills for hypertension	20369	(9.38%)	5067	(13.21%)	15302	(8.56%)

Outcome	Age: 50-54		55-59		60-69		70-79	
Number randomized	9191		14664		31390		12890	
Mean follow-up (months)	44.5		40.6		36.4		35.7	
Hospitalizations								
Ever	1729	(5.08%)	2908	(5.86%)	7709	(8.09%)	4061	(10.60%)
Two or more	571	(1.68%)	972	(1.96%)	2767	(2.90%)	1671	(4.36%)
Other								
DVT[2]	30	(0.09%)	53	(0.11%)	171	(0.18%)	112	(0.29%)
PE	12	(0.04%)	21	(0.04%)	72	(0.08%)	58	(0.15%)
Diabetes (treated)	473	(1.39%)	864	(1.74%)	1964	(2.06%)	852	(2.22%)
Gallbladder disease[3]	381	(1.12%)	603	(1.22%)	1192	(1.25%)	445	(1.16%)
Hysterectomy[4]	143	(0.73%)	210	(0.68%)	426	(0.78%)	182	(0.85%)
Glaucoma	273	(0.80%)	514	(1.04%)	1550	(1.63%)	860	(2.24%)
Osteoporosis	506	(1.49%)	1015	(2.05%)	3074	(3.23%)	1794	(4.68%)
Osteoarthritis[5]	985	(3.22%)	1891	(4.16%)	4870	(5.51%)	2571	(7.16%)
Rheumatoid arthritis	279	(0.82%)	486	(0.98%)	951	(1.00%)	443	(1.16%)
Intestinal polyps	420	(1.23%)	795	(1.60%)	2049	(2.15%)	914	(2.39%)
Lupus	59	(0.17%)	84	(0.17%)	171	(0.18%)	50	(0.13%)
Kidney Stones[5]	97	(0.46%)	168	(0.51%)	367	(0.55%)	137	(0.51%)
Cataracts[5]	380	(1.79%)	1157	(3.54%)	5282	(7.91%)	3266	(12.11%)
Pills for hypertension	2079	(6.11%)	3801	(7.67%)	9581	(10.06%)	4908	(12.81%)

[1] Participants with unmarked ethnicity are classified as Minority.

[2] Inpatient DVT only.

[3] "Gallbladder disease" includes self-reports of both hospitalized and non-hospitalized events.

[4] Only women without a baseline hysterectomy are used to compute the annual rates of hysterectomy.

[5] These outcomes have not been self-reported on all versions of Form 33. The annualized percentages are corrected for the different amounts of follow-up.

Table 6.9
Locally Confirmed Other Cancers[1]: CT and OS Participants

Data as of: February 29, 2000

	CT		OS	
Number of participants providing Form 33	68135		93721	
Mean follow-up time (months)	38.3		31.5	
Ppts with other cancer	830	(0.38%)	880	(0.36%)
Adrenal gland	1	(<0.01%)	3	(<0.01%)
Anus	3	(<0.01%)	6	(<0.01%)
Biliary tract	12	(0.01%)	9	(<0.01%)
Bladder	48	(0.02%)	46	(0.02%)
Bones/joints/articular cartilage (limbs)	2	(<0.01%)	1	(<0.01%)
Bones/joints/articular cartilage (other)	2	(<0.01%)	1	(<0.01%)
Brain	22	(0.01%)	27	(0.01%)
Cervix	27	(0.01%)	10	(<0.01%)
Connective/subcutaneous/soft tissues	3	(<0.01%)	3	(<0.01%)
Endocrine gland, related structures	1	(<0.01%)	1	(<0.01%)
Esophagus	5	(<0.01%)	9	(<0.01%)
Eye and adnexa	3	(<0.01%)	2	(<0.01%)
Genital organs	11	(0.01%)	6	(<0.01%)
Kidney	40	(0.02%)	43	(0.02%)
Larynx	4	(<0.01%)	1	(<0.01%)
Leukemia	41	(0.02%)	27	(0.01%)
Liver	9	(<0.01%)	11	(<0.01%)
Lung (bronchus)	154	(0.07%)	185	(0.08%)
Lymph nodes	6	(<0.01%)	2	(<0.01%)
Lymphoma, Hodgkins disease	3	(<0.01%)	2	(<0.01%)
Lymphoma, non-Hodgkins	66	(0.03%)	78	(0.03%)
Melanoma of the skin	108	(0.05%)	127	(0.05%)
Multiple myeloma	32	(0.01%)	25	(0.01%)
Oral (mouth)	6	(<0.01%)	5	(<0.01%)
Palate	2	(<0.01%)	2	(<0.01%)
Pancreas	51	(0.02%)	45	(0.02%)
Parotid gland (Stensen's duct)	2	(<0.01%)	5	(<0.01%)
Peripheral nerves and autonomic nervous system	0	(0.00%)	1	(<0.01%)
Respiratory system, intrathoracic	1	(<0.01%)	2	(<0.01%)
Salivary glands	1	(<0.01%)	2	(<0.01%)
Stomach	6	(<0.01%)	7	(<0.01%)
Thyroid	27	(0.01%)	31	(0.01%)
Tongue	9	(<0.01%)	5	(<0.01%)
Urinary organs	1	(<0.01%)	6	(<0.01%)
Uterus, not specified	14	(0.01%)	21	(0.01%)
Other/unknown site of cancer	117	(0.05%)	132	(0.05%)

[1] No reported cases of accessory sinus or pyriform sinus cancers.

Table 6.10
Locally Confirmed Other Fractures: CT and OS Participants

Data as of: February 29, 2000

	CT	OS[1]
Locally Confirmed		
Number of participants providing Form 33	68135	7203
Mean follow-up time (months)	38.3	37.3
Ppts with other fractures	2,830 (1.30%)	293 (1.31%)
Ankle	476 (0.22%)	42 (0.19%)
Carpal bone(s) in wrist	63 (0.03%)	5 (0.02%)
Clavicle or collar bone	40 (0.02%)	8 (0.04%)
Humerus, shaft/unspecified	24 (0.01%)	3 (0.01%)
Humerus, upper end	262 (0.12%)	25 (0.11%)
Humerus, lower end	33 (0.02%)	3 (0.01%)
Metacarpal bone(s)	101 (0.05%)	6 (0.03%)
Patella	114 (0.05%)	18 (0.08%)
Pelvis	83 (0.04%)	17 (0.08%)
Radius or ulna	803 (0.37%)	80 (0.36%)
Sacrum and coccyx	24 (0.01%)	4 (0.02%)
Scapula	14 (0.01%)	2 (0.01%)
Shaft of femur	33 (0.02%)	2 (0.01%)
Tarsal/metatarsal bones	485 (0.22%)	52 (0.23%)
Tibia and fibula	253 (0.12%)	21 (0.09%)
Tibial plateau	56 (0.03%)	4 (0.02%)
Upper radius/ulna	155 (0.07%)	18 (0.08%)
Unknown other fracture	2 (0.00%)	0 (0.00%)
Self-Reports		
Number of participants providing Form 33		93721
Mean follow-up time (months)		31.5
Upper Leg		101 (0.04%)
Pelvis		162 (0.07%)
Knee		265 (0.11%)
Upper Arm		416 (0.17%)
Lower Arm		1140 (0.46%)
Hand		160 (0.07%)
Lower Leg		928 (0.38%)
Foot		822 (0.33%)
Tailbone		53 (0.02%)
Elbow		213 (0.09%)
Vertebra		453 (0.18%)
Other Fracture		1192 (0.49%)

[1] Other fractures for OS Participants are only confirmed in the three bone density clinics.

Table 6.11
Cross-tabulation of ECG Codes Suggesting an Incident MI and Locally Confirmed and Self-Reported MI for all CT participants

Data as of: February 29, 2000

	No Locally Confirmed MI or Open Self-Report of MI	Open Self-Report of MI[1]	Locally Confirmed MI[2]	Total
All CT Participants				
No significant Q or ST-T evolution[3]	29654	9	172	29835
Borderline Q-wave change[4]	831	3	21	855
Ischemic ST-T evolution[5]	479	2	26	507
Possible evolving Q-wave MI[6]	70	1	12	83
Evolving Q-wave MI[7]	14[8]	0	11	25
Total	31048	15	242	31305
HRT Participants				
No significant Q or ST-T evolution[3]	10935	3	75	11013
Borderline Q-wave change[4]	328	1	8	337
Ischemic ST-T evolution[5]	209	1	8	218
Possible evolving Q-wave MI[6]	29	0	5	34
Evolving Q-wave MI[7]	5[8]	0	5	10
Total	11506	5	101	11612
DM Participants				
No significant Q or ST-T evolution[3]	22341	7	123	22471
Borderline Q-wave change[4]	598	2	15	615
Ischemic ST-T evolution[5]	340	2	20	362
Possible evolving Q-wave MI[6]	48	1	10	59
Evolving Q-wave MI[7]	11[8]	0	6	17
Total	23338	12	174	23524
CaD Participants				
No significant Q or ST-T evolution[3]	16867	4	64	16935
Borderline Q-wave change[4]	491	2	9	502
Ischemic ST-T evolution[5]	249	1	5	255
Possible evolving Q-wave MI[6]	42	1	4	47
Evolving Q-wave MI[7]	10[8]	0	6	16
Total	17659	8	88	17755

[1] Includes only self-reports of events before the year 3 ECG.
[2] Includes only locally confirmed MIs that took place before the year 3 ECG.
[3] Novacode Incident MI code 1.5.0
[4] Novacode Incident MI code 1.5.7
[5] Novacode Incident MI code 1.5.5, 1.5.6.1, and 1.5.6.2
[6] Novacode Incident MI code 1.5.3 and 1.5.4
[7] Novacode Incident MI code 1.5.1 and 1.5.2
[8] Cases in this cell are potentially the silent MIs.

Table 6.12
Cause of Death: CT and OS Participants (Annualized Percentages)

Data as of: February 29, 2000

	CT		OS	
Number Randomized	68135		93721	
Mean Follow-up Time (months)	38.3		31.5	
Total death	773	(0.36%)	1097	(0.45%)
Adjudicated death	648	(0.30%)	897	(0.37%)
Final Adjudicated Death	615	(0.28%)	799	(0.33%)
Temporary Adjudicated Death	33	(0.02%)	98	(0.04%)
Cardiovascular				
Athereosclerotic cardiac	98	(0.05%)	93	(0.04%)
Cerebrovascular	46	(0.02%)	64	(0.03%)
Other cardiovascular	59	(0.03%)	61	(0.02%)
Unknown cardiovascular	15	(0.01%)	15	(0.01%)
Total cardiovascular deaths	218	(0.10%)	233	(0.09%)
Cancer				
Breast cancer	3	(<0.01%)	52	(0.02%)
Ovarian cancer	18	(0.01%)	31	(0.01%)
Endometrial cancer	3	(<0.01%)	8	(0.01%)
Colorectal cancer	33	(0.02%)	42	(0.02%)
Other cancer	227	(0.10%)	281	(0.11%)
Unknown cancer site	15	(0.01%)	29	(0.01%)
Total cancer deaths	299	(0.14%)	443	(0.18%)
Accident/injury				
Homicide	4	(<0.01%)	3	(<0.01%)
Accident	23	(0.01%)	24	(0.01%)
Suicide	2	(<0.01%)	9	(<0.01%)
Other injury	3	(<0.01%)	2	(<0.01%)
Total accidental deaths	32	(0.01%)	38	(0.02%)
Other				
Other known cause	55	(0.03%)	115	(0.05%)
Unknown cause	33	(0.02%)	56	(0.02%)
Total deaths – other causes	88	(0.04%)	171	(0.07%)

Table 6.13
Lost-to-Follow-up and Vital Status by Clinic: CT Participants

Data as of: February 29, 2000

	Deceased		Alive: Current Participation[1]		Alive: Recent Participation[2]		Alive: Past/Unknown Participation[3]		Stopped Follow-up[4]		Lost to Follow-up[5]		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N
Clinic													
VCCs													
Atlanta	25	1.5	1609	93.7	32	1.9	4	0.2	11	0.6	36	2.1	1717
Birmingham	40	2.2	1743	95.1	20	1.1	0	0.0	15	0.8	14	0.8	1832
Bowman	13	0.9	1458	96.3	13	0.9	0	0.0	5	0.3	25	1.7	1514
Brigham	23	1.0	2247	97.4	22	1.0	1	<0.1	1	<0.1	14	0.6	2308
Buffalo	23	1.4	1551	96.3	17	1.1	1	0.1	10	0.6	9	0.6	1611
Chicago	32	2.0	1499	92.5	27	1.7	4	0.2	30	1.9	28	1.7	1620
Iowa City	30	1.2	2371	97.5	12	0.5	0	0.0	8	0.3	12	0.5	2433
La Jolla	28	1.3	2006	93.6	42	2.0	1	<0.1	6	0.3	61	2.8	2144
Memphis	29	1.7	1601	91.9	51	2.9	0	0.0	15	0.9	47	2.7	1743
Minneapolis	26	1.3	1903	95.6	50	2.5	0	0.0	3	0.2	8	0.4	1990
Newark	29	1.2	2286	92.8	52	2.1	0	0.0	64	2.6	33	1.3	2464
Pawtucket	27	1.0	2513	94.8	27	1.0	0	0.0	41	1.5	42	1.6	2650
Pittsburgh	24	1.4	1601	96.5	16	1.0	0	0.0	11	0.7	7	0.4	1659
Seattle	27	1.5	1704	95.3	26	1.5	7	0.4	21	1.2	3	0.2	1788
Tucson	35	1.7	1857	90.8	62	3.0	0	0.0	45	2.2	47	2.3	2046
U.C. Davis	35	1.9	1772	94.2	34	1.8	4	0.2	7	0.4	29	1.5	1881
NCCs													
Chapel Hill	15	1.0	1494	97.1	6	0.4	0	0.0	15	1.0	8	0.5	1538
Chi-rush	17	1.3	1243	93.5	19	1.4	0	0.0	27	2.0	24	1.8	1330
Cincinnati	7	0.5	1205	86.3	99	7.1	3	0.2	27	1.9	55	3.9	1396
Columbus	22	1.4	1505	96.5	1	0.1	0	0.0	22	1.4	10	0.6	1560
Detroit	5	0.4	1153	83.6	103	7.5	0	0.0	70	5.1	49	3.6	1380
Gainesville	23	1.1	1948	95.5	18	0.9	1	<0.1	28	1.4	21	1.0	2039
GWU-DC	9	0.6	1467	96.8	17	1.1	0	0.0	6	0.4	16	1.1	1515
Honolulu	8	0.6	1281	91.0	56	4.0	1	0.1	20	1.4	42	3.0	1408
Houston	5	0.4	1173	92.9	46	3.6	0	0.0	31	2.5	8	0.6	1263
Irvine	13	0.8	1492	92.2	50	3.1	3	0.2	34	2.1	27	1.7	1619
L.A.	14	0.8	1594	93.9	39	2.3	1	0.1	27	1.6	23	1.4	1698
Madison	15	1.0	1506	96.9	6	0.4	0	0.0	19	1.2	8	0.5	1554
Medlantic	19	1.3	1392	92.7	47	3.1	0	0.0	21	1.4	22	1.5	1501
Miami	11	0.7	1265	85.4	72	4.9	0	0.0	27	1.8	107	7.2	1482
Milwaukee	16	1.0	1548	93.6	62	3.7	0	0.0	21	1.3	7	0.4	1654
Nevada	25	1.7	1458	97.6	2	0.1	0	0.0	7	0.5	2	0.1	1494
NY-City	16	0.8	1692	89.6	110	5.8	0	0.0	12	0.6	58	3.1	1888
Oakland	14	0.9	1524	96.3	24	1.5	1	0.1	12	0.8	7	0.4	1582
Portland	20	1.2	1503	92.5	50	3.1	2	0.1	25	1.5	25	1.5	1625
San Antonio	5	0.4	1251	90.7	21	1.5	4	0.3	52	3.8	46	3.3	1379
Stanford	16	0.9	1755	96.7	12	0.7	0	0.0	17	0.9	15	0.8	1815
Stonybrook	11	0.8	1317	97.2	2	0.1	0	0.0	18	1.3	7	0.5	1355
Torrance	10	1.0	887	86.5	72	7.0	8	0.8	16	1.6	32	3.1	1025
Worcester	11	0.7	1566	95.8	41	2.5	0	0.0	4	0.2	13	0.8	1635
Total	773	1.1	63940	93.8	1478	2.2	46	0.1	851	1.2	1047	1.5	68135

[1] Participants who have filled in a Form 33 within the last 9 months.

[2] Participants who last filled in a Form 33 between 9 and 18 months ago.

[3] Participiants without a Form 33 within the last 18 months, who have been located (as indicated on Form 23) within the last 6 months.

[4] Participants with codes 5 (no follow-up) or 8 (absolutely no follow-up) on Form 7.

[5] Participants not in any of the above categories.

Table 6.14
Lost-to-Follow-up and Vital Status by Clinic: OS Participants

Data as of: February 29, 2000

	Deceased		Alive: Current Participation[1]		Alive: Recent Participation[2]		Alive: Past/Unknown Participation[3]		Stopped Follow-up[4]		Lost to Follow-up[5]		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N
Clinic													
VCCs													
Atlanta	26	1.1	2282	92.3	138	5.6	0	0.0	4	0.2	23	0.9	2473
Birmingham	47	1.9	2260	89.4	175	6.9	0	0.0	17	0.7	30	1.2	2529
Bowman	26	1.2	2111	95.0	34	1.5	0	0.0	19	0.9	33	1.5	2223
Brigham	13	0.4	2814	95.4	99	3.4	1	0.0	0	0.0	22	0.7	2949
Buffalo	50	2.2	2114	94.0	51	2.3	0	0.0	6	0.3	27	1.2	2248
Chicago	25	1.3	1765	93.2	59	3.1	8	0.4	9	0.5	27	1.4	1893
Iowa City	22	0.7	3012	96.6	54	1.7	0	0.0	10	0.3	21	0.7	3119
La Jolla	40	1.2	3138	90.6	184	5.3	0	0.0	8	0.2	92	2.7	3462
Memphis	25	1.0	2061	81.9	299	11.9	9	0.4	17	0.7	107	4.2	2518
Minneapolis	21	0.8	2611	95.9	58	2.1	3	0.1	13	0.5	17	0.6	2723
Newark	33	1.0	2963	87.8	249	7.4	0	0.0	25	0.7	105	3.1	3375
Pawtucket	45	1.3	3315	92.3	163	4.5	0	0.0	15	0.4	53	1.5	3591
Pittsburgh	33	1.7	1785	93.2	66	3.4	0	0.0	4	0.2	28	1.5	1916
Seattle	32	1.9	1540	92.7	66	4.0	2	0.1	11	0.7	10	0.6	1661
Tucson	47	1.7	2484	89.8	126	4.6	0	0.0	24	0.9	85	3.1	2766
U.C. Davis	30	1.3	2147	95.1	40	1.8	13	0.6	8	0.4	19	0.8	2257
NCCs													
Chapel Hill	19	0.9	1997	95.9	55	2.6	0	0.0	4	0.2	7	0.3	2082
Chi-rush	13	0.6	1741	84.7	210	10.2	0	0.0	19	0.9	72	3.5	2055
Cincinnati	20	0.9	2010	89.4	140	6.2	8	0.4	6	0.3	64	2.8	2248
Columbus	23	1.0	2129	95.7	53	2.4	6	0.3	6	0.3	8	0.4	2225
Detroit	17	0.8	1772	83.9	208	9.9	0	0.0	39	1.8	75	3.6	2111
Gainesville	30	1.1	2594	93.1	85	3.0	3	0.1	35	1.3	40	1.4	2787
GWU-DC	32	1.4	2158	96.0	51	2.3	2	0.1	1	0.0	5	0.2	2249
Honolulu	17	0.8	1914	90.5	104	4.9	1	0.0	28	1.3	50	2.4	2114
Houston	27	1.3	1913	89.9	99	4.7	0	0.0	28	1.3	60	2.8	2127
Irvine	29	1.3	2071	92.9	59	2.6	0	0.0	34	1.5	36	1.6	2229
L.A.	10	0.5	2087	95.1	64	2.9	2	0.1	15	0.7	16	0.7	2194
Madison	32	1.6	1914	96.4	21	1.1	1	0.1	7	0.4	10	0.5	1985
Medlantic	18	0.8	1927	87.9	148	6.8	5	0.2	1	0.0	93	4.2	2192
Miami	15	1.1	1087	77.4	129	9.2	15	1.1	6	0.4	153	10.9	1405
Milwaukee	19	0.8	2023	89.8	180	8.0	0	0.0	6	0.3	24	1.1	2252
Nevada	61	2.8	2074	95.1	37	1.7	0	0.0	7	0.3	2	0.1	2181
NY-City	29	1.0	2434	83.9	231	8.0	1	0.0	12	0.4	193	6.7	2900
Oakland	34	1.7	1947	94.9	43	2.1	7	0.3	10	0.5	11	0.5	2052
Portland	18	0.8	2087	93.7	91	4.1	3	0.1	16	0.7	13	0.6	2228
San Antonio	15	0.8	1694	87.3	139	7.2	4	0.2	25	1.3	64	3.3	1941
Stanford	36	1.3	2545	94.6	61	2.3	1	0.0	30	1.1	18	0.7	2691
Stonybrook	21	1.0	1924	94.9	58	2.9	0	0.0	9	0.4	16	0.8	2028
Torrance	21	1.4	1242	82.6	149	9.9	34	2.3	14	0.9	44	2.9	1504
Worcester	26	1.2	2111	94.3	86	3.8	0	0.0	4	0.2	11	0.5	2238
Total	1097	1.2	85797	91.5	4362	4.7	129	0.1	552	0.6	1784	1.9	93721

[1] Participants who have filled in a Form 33 within the last 15 months.

[2] Participants who last filled in a Form 33 between 15 and 24 months ago.

[3] Participants without a Form 33 within the last 18 months, who have been located (as indicated on Form 23) within the last 6 months.

[4] Participants with codes 5 (no follow-up) or 8 (absolutely no follow-up) on Form 7.

[5] Participants not in any of the above categories.

7. Clinical Center Performance Monitoring

7.1 Performance Monitoring

A four step plan is used to identify clinic-specific performance issues in a timely fashion, to reinforce good performance, and to provide assistance or institute corrective action if performance is inadequate.

7.2 PMC Committee Activity

In July 1998, the PMC separated its monitoring activities into two separate groups, with one group addressing outcomes and one group addressing adherence/retention and other issues. Membership of the Adherence/Retention PMC (A&R PMC) includes: Sally Shumaker, CFC, chair; Shirley Beresford, Seattle Clinical Center; Judith Hsia, George Washington Clinical Center (replacing Cheryl Ritenbaugh, Portland Clinical Center, in November); Linda Pottern, Project Office; and Andrea LaCroix (replacing Ross Prentice in November), Barb Cochrane, Lesley Tinker, Julie Hunt and Bernedine Lund, CCC. Membership of the Outcomes PMC includes Anne McTiernan, CCC, chair; David Curb, Honolulu Clinical Center, Marian Limacher, Gainesville Clinical Center; Ron Prineas, CFC (replacing Curt Furberg, CFC, in January); Jacques Rossouw, Project Office; and Bernedine Lund, CCC.

Since September 1, 1999, the A&R PMC held one conference call every 4-6 weeks, reviewing 5-6 Clinical Centers on each call. Information reviewed about each Clinical Center includes: DM Triage System Adherence Levels; comparison of performance to goals as well as to Clinical Center averages; and task completeness. The committee conducted three Level 4 visits since September 1. Three additional Level 4 visits are planned for the spring 2000.

In the spring of 1999, the A&R PMC repeated its requests to Clinical Centers for examples of strategies the clinics found successful. In October 1999, the PMC began developing a summary of these strategies and plans to share the list with all Clinical Centers.

In the same period, the Outcomes PMC also held one conference call per month, reviewing 5-6 Clinical Centers on each call. A summary of each Clinical Center included: 1) recent and cumulative data on collection of required forms, outcomes packet assembly, and local adjudication; 2) a graph showing the timeliness of outcomes processing over time; and 3) a summary of number of staff and local adjudicators. A newly developed report identifying and classifying participants based on follow-up status and vital status was added to the review materials in February. After learning that one Clinical Center had modified the outcomes collection forms, the CCC members of the Outcomes PMC held a conference call in December with that Clinical Center to discuss plans for collection of potential missing outcomes. In December, the PMC recommended that Dr. Lenfant send a letter to those Clinical Centers showing good work and/or improvement in their processing of outcomes, and the Outcomes PMC send a letter to the other Clinical Centers, which are performing poorly, to indicate that further improvement is needed.

8. Other Study Activities

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

Table 8.1 – Publications presents current and proposed publications that have been approved by the Publications and Presentations Committee.

Table 8.2 – Ancillary Studies lists all ancillary study proposals received by the Design and Analysis Committee along with some key features of the studies and their current status.

These tables represent the current information available to the relevant committees. Updates are clearly needed. Status reports for either papers or ancillary studies may be sent to the CCC, attention Sundara Murphy. The CCC requests one reprint from each published manuscript for study archives.

Table 8.1

Publications

MS ID	Title	Authors	Data Focus	Stage	Reference
1	Informed Consent in the Women's Health Initiative Clinical Trial and Observational Study	**McTiernan**, Rossouw, Manson, Franzi, Taylor, Carleton, Johnson, Nevitt	Gen.	10	Journal of Women's Health 4(5):519-29, 1995
4	The Women's Health Initiative: Overview of the Nutrition Component	**Tinker**, Burrows, Henry, Patterson, Van Horn, Rupp	Gen.	10	Nutrition and Women's Health, pp. 510-542, 1996.
5	Women Health Initiative: Why Now? What is it? What's New?	**Matthews**, Shumaker, Bowen, Langer, Hunt, Kaplan, Klesges, Ritenbaugh	Gen.	10	American Psychologist. 52(2):101-116, 1997 Feb.
6	Low-fat Diet Practices of Older Women: "Prevalence and Implication for Dietary Assessment"	**Patterson**, Kristal, Coates, Ritenbaugh, Van Horn, Caggiula, Snetselaar, Tylavsky	Gen.	10	Journal of the American Dietetic Association. 96(7):670-9, 1996 Jul.
7	The Evolution of the Women's Health Initiative: Perspectives from the NIH	**Rossouw**, Pinn, Clifford, McGowan	Gen.	10	Journal of the American Medical Women's Association. 50(2):50-5, 1995 Mar-Apr
8	Design of the WHI Clinical Trial and Observational Study	**WHI Study Group publication writing group:** Prentice, Rossouw, Furberg, Johnson, Henderson, Cummings, Manson, Freedman, Oberman, Kuller, Anderson	Gen.	10	Controlled Clinical Trials 19:61-109, 1998
9	Approaches to Monitoring the Results of Long-term Disease Prevention Trials: Examples from the Women's Health Initiative	**Freedman**, Anderson, Kipnis, Prentice, Wang, Rossouw, Wittes, DeMets	CT	10	Controlled Clinical Trials. 17(6):509-25, 1996 Dec.
11	The Role of Randomized Controlled Trials in Assessing the Benefits and Risks of Long-term Hormone Replacement Therapy: Example of the Women's Health Initiative	**Prentice**, Rossouw, Johnson, Freedman, McTiernan	CT	10	Menopause 3(2):71-76, 1996
21	Factors Associated with Prevalence, Treatment and Control of Hypertension among Post-menopausal Women: Baseline Data from the Women's Health Initiative	**Wassertheil-Smoller**, Manson, Wong, Lasser, Kotchen, Langer, Grimm, Black, Psaty, Anderson, Francis	OS	10	Hypertension to appear
24	Estimation of the Correlation between Nutrient Intake Measures Under Restricted Sampling	**Wang**, Anderson, Prentice	Gen.	10	Biometrics 55:711-717, 1999
27	The Effects of Insurance Coverage and Ethnicity on Mammography Utilization in a Postmenopausal Population	**Bush**, Langer	Gen.	10	Western Journal of Medicine 168:236-40, 1998
35	Measurement Characteristics of the WHI Food Frequency Questionnaire	**Patterson**, Kristal, Carter, Inker, Bolton, Agurs-Collins	Gen.	10	Annals of Epidemiology 1999:9:178-197

MS ID	Title	Authors	Data Focus	Stage	Reference
37	Depression as Mediated by Social Support, Life Events, and Sexual Activity in Postmenopausal Non-Hispanic White and Latina Women	**Larisch**, Talavera, Langer, Velasquez, Elder	Gen.	10	
40	The Health Impact of Domestic Violence in Older Women	**Mouton**, Furniss, Lasser, Rovi	OS	10	Journal of Women's Health & Gender-Based Medicine 1999:8(9):1173-1179
60	WHIMS: a Trial of the Effect of Estrogen Therapy in Preventing and Slowing the Progression of Dementia	**Shumaker**, Bowen	WHIMS	10	Controlled Clinical Trials 19:604-621
63	Health Insurance as a Determinant of Cancer Screening in WHI OS Participants	**Hsia**, Kemper, Bowen, Zapka, Mason, Lillington, Limacher, Kiefe, Sofaer, Pettinger	OS	10	Preventive Medicine, In Press
71	The Women's Health Initiative: Goals, Rationale, and Current Status	**Liu**	Gen.	10	Menopausal Medicine, Vol.6(2), p.1-4, 1998
103	The Women's Health Initiative: Recruitment Complete - Looking Back and Looking Forward (Guest Editorial)	**Rossouw**, Hurd	CT	10	Journal of Women's Health 8:3-5, 1999.
10	A Comprehensive Data Management System for Multicenter Studies	**Anderson**, Davis, Koch	Gen.	9	
12	Factors Associated with Insurance Status among Participants in the WHI	**Hsia**, Sofaer, Kiefe, Zapka, Bowen, Mason, Limacher, Pettinger, Lillington	Gen.	9	
17	Sexual Orientation and Health: Comparisons in the Women's Health Initiative Sample	**Valanis**, Charney, Whitlock, Wassertheil-Smoller, Bassford, Bowen, Carter	CT	9	
30	Completeness of Purchase Mailing Lists for Identifying Older Women	**Falkner**, Wactawski-Wende, Trevisan	CT	9	
61	WHI Halfway Paper (100K Paper)	**Langer**, Kotchen, Daugherty, Lewis, Elmer, Trevisan, Noonan, Hendrix, Adams-Campbell	Gen.	9	
69	Correlates of Serum Lypocene in Older Women	**Casso**, White, Patterson, Agurs-Collins, Kooperberg, Haines	CT	9	
72	Post-Menopausal Bone Loss and its Relationship to Oral Bone Loss	**Jeffcoat**, Lewis, Reddy, Wang, Redford	Gen.	9	Periodontics 2000
88	Estimating Normal Hemogram Values for Postmenopausal Women	**Carleton**, Assaf, Miller	Gen.	9	
93	Fat Intake in Husbands of Women in the Dietary Component of the Women's Health Initiative	**Shikany**	Gen.	9	
26	Special Populations Recruitment for the WHI: Success and Limitations	**Fouad**, Corbie-Smith, Curb, Howard, Mouton, Simon, Talavera, Thompson, Wang, White, Young	Gen.	8	

MS ID	Title	Authors	Data Focus	Stage	Reference
70	Correlates of Serum A- and G-Tocopherol in the WHI	**White**, Masaki, Chen, Shikany, Caan, Mares-Perlman, Wilson, Kristal	CT	8	
76	Labeling as a Predictor of Dietary Maintenance	**Hopkins**, Burrows, Bowen, Tinker	CT	8	
85	Women's Health Initiative: Rationale, Design and Progress Report	**Johnson**, Anderson, Barad, Stefanick, McNagy	CT	8	Journal of the British Menopause Society 5:155-159, 2000
104	Promoting Adherence and Retention to Clinical Trials in Special Populations: A Women's Health Initiative Workshop	**Wilcox**, Shumaker, Bowen, Naughton, Rosal, Ludlam, Dugan, Hunt, Stevens	Gen.	8	
105	Retention of Low Income and Minority Women in Clinical Trials: A Focus Group Study	**Johnson**, Williams, Fouad	CT	8	
108	Cross-Sectional Geometry and Bone Mass in the Proximal Femur in African-American and White Postmenopausal Women	**Nelson**, Hendrix	CT	8	
109	NCI Monograph: Approaches to Research Trials Recruitment in Hispanic Communities: Review and Recommendations	**Larkey**	Gen.	8	
111	Effects of Fat Intake on Fat Hedonics: Cognition or Taste?	**Bowen**, Green, Vizenor, Vu, Kreuter, Rolls	OS	8	
112	Results of an Adjunct Dietary Intervention Program in the Women's Health Initiative	**Bowen**, Ehret, Pedersen, Snetselaar, Johnson, Tinker, Hollinger, Lichty, Sivertsen, Ocken, Staats, Beedoe	OS	8	
43	Sleep Complaints of Postmenopausal Women	**Kripke**, Freeman, Masaki, Brunner, Jackson, Hendrix, Carter	CT	7	
73	Innovative Strategies for Monitoring and Enhancing Clinic Performance in the WHI Clinical Trial: The Creation of the Performance Monitoring Committee	**Pottern**, Naughton, Lund, Cochrane, Brinson, Kotchen, McTiernan, Shumaker	Gen.	7	
14	Psychosocial and Behavioral Correlates of Moderate Alcohol Consumption in Women	**Powell**, Hymowitz, Criqui, Ockene, Finnegan, Castro, Trevisan, Curb, Hunt	CT	6	
19	Body Weight and Anthropometric Measures of Adiposity	**Manson**, Kotchen, Perri, Lewis, Johnson, Freed, Hall, Allen, Foreyt, Tinker, Stefanick	Gen.	6	
22	Prevalence of Pelvic Organ Prolapse and Urinary Incontinence in Women	**Clark**, Harris, Varner, Chang, Hendrix, Barnabei, Mattox, McTiernan, Francis, Nygaard	CT	6	
34	The Relationship between Smoking Status, Body Weight, and Waist-to-Hip Ratio: the WHI	**Johnson**, Klesges, Hays, Manson, Curb, Black, Liu	Gen.	6	

MS ID	Title	Authors	Data Focus	Stage	Reference
59	Dietary and Supplemental Calcium Intake and the Occurrence of Kidney Stones in Postmenopausal Women Residing in the Kidney Stone Belt	**Hall**, Oberman, Hays, Paskett, Limacher, Johnson, Watts, Pettinger	Gen.	6	
62	Self-reported Urogenital Symptoms in Postmenopausal Women aged 50-79: WHI	**Pastore**, Hulka, Wells, Carter	Gen.	6	
79	Databased Tracking and Statistical Models of the Clinical Trial Recruitment Process	**Creech**	CT	6	
13	Cardiovascular and other Physiological Correlates of Depression	**Wassertheil-Smoller**, Talavera, Campbell, Shumaker, Ockene, Robbins, Dunbar, Greenland, Cochrane	Gen.	5	
16	An Examination of the Differences in Total Energy and Several Nutrient Scores Derived from the FFQ vs. Estimates Based on Basal Metabolic Requirements and Food Record - Derived Scores in the WHI	**Hebert**, Beresford, Patterson, Chlebowski, St. Jeor, Coates, Elmer, Hartman, Prentice, Ebbeling	Gen.	5	
25	Hormone Replacement Therapy Effects on the Resting ECG	**Greenland**, Daugherty, Frishman, Kadish, Limacher, Schwartz	CT	5	
31	Comparisons between Never Smokers, Former Smokers, and Current Smokers in the WHI	**Hymowitz**, Ockene, Bowen, Robbins, Brunner, Shikany, Wagenknecht	OS	5	
36	Prevalence of Silent MI	**Sagar**, Kotchen, Wong, Graettinger, Burke, Van Vorhees, McIntosh	CT	5	
38	The Relationship of Selected Dietary Components and Risk of Adenoma and Colorectal Cancer among Postmenopausal Women: WHI	**Frank**, Agurs-Collins, Gams, Garland, Khandekar, Paskett, Wylie-Rosett, Pettinger	Gen.	5	
41	Determinants of Fasting Hyperinsulinemia	**Manson**, LaCroix, Haan, Rodrigues, Wagenknecht, Johnson, Allen, Hendrix	Gen.	5	
44	Effect of Hysterectomy with Ovarian Reservation on Cardiovascular Morbidity and Mortality	**Brzyski**, Barnabei, Barad, Giudice, Satterfield, Margolis, McNeeley	CT	5	
49	Patterns of Use and Characteristics Associated with HRT among Postmenopausal Women	**Dunn**, Greenland, Woods, Stovall, Bartholow, Francis	Gen.	5	
51	The Relationship of Quality of Social Support to Frequency of Cancer Screening Behaviors among Postmenopausal Women	**Lane**, Taylor, Glanz, Elam, Klaskala, Powell, Messina, Smith	Gen.	5	
52	Nutrient Intake of Women with Diabetes in the WHI Observational Study Cohort	**Tinker**, Gams, Lee, Smith, West, Snetselaar, Caggiula	Gen.	5	
53	Dietary, Physical Activity, and Exercise Patterns among Diabetics	**Agurs-Collins**, Adams-Campbell, Passaro, Howard	Gen.	5	

MS ID	Title	Authors	Data Focus	Stage	Reference
57	Regional Differences in Stroke Morbidity at Baseline in the WHI	**Johnson**, Hall, Oberman, Sheps, Hulka, Hays, Baum, Schenken, Burke, Limacher, Anderson, Jeppson	Gen.	5	
67	Association of Yogurt Consumption to Breast and Colorectal Cancers Among WHI Participants in the OS	**Mossavar-Rahmani**, Vitolins, Parker, Wodarski, Hebert, Caan, Himes, Garland, Kristal	OS	5	
74	Baseline Characteristics of the WHI-OS Breast Cancer Survivor Cohort	**Paskett**, Sherman, Anderson, Hays, McDonald, Naughton	OS	5	
83	Physical Activity and Risk of Breast Cancer in Postmenopausal Women: the Women's Health Initiative	**McTiernan**, Wilcox, Coates, Woods, Ockene, Adams-Campbell, White, Kooperberg	Gen.	5	
86	Adherence Factors in the Dietary Modification Clinical Trial	**Tinker**, Perri, Bowen, Patterson, Parker, Wodarski, McIntosh, Sevick	CT	5	
87	Incidence and Correlates of Hip and Knee Replacement in the WHI	**Wallace**, White, Chang, Nevitt, LaCroix, Kaplan, Sturm	Gen.	5	
98	Patterns of Antioxidant Supplement Use in Participants in the Women's Health Initiative	**Anderson**, Dunn, Patterson, Agurs-Collins, Shikany	Gen.	5	
120	Anthropometrics and Risk of Breast Cancer in Postmenopausal Women: The WHI	**Morimoto**, White, McTiernan, Chlebowski, Hays, Stefanick, Margolis, Manson, Kuller, Chen, Muti, Lopez	OS	5	
122	HMG Co-A Reductase Inhibitor (Statin) Use and Risk of Fracture In the Women's Health Initiative Observational Study	LaCroix, Jackson, Cauley, Chen, Lewis, McGowan, Hsia, Daugherty, McNeeley, Passaro, Bauer	OS	5	
20	Correlates of Endogenous Sex Hormone Concentrations in WHI	**McTiernan**, Wactawski-Wende, Chen, Meilahn, La Valluer, Cummings, Hiaat, Baum, Hulka, Wang, McNagny	CT	4	
23	A Comparative Analysis of Predictors of Recruitment for Hispanic and Caucasian Women in the WHI	**Talavera**, Fouad, Howard, Satterfield, Schenken, Simon, Porter, Bonk, Hunt, Wang, Corbie-Smith	Gen.	4	
39	Interactions among HRT and Dietary Fat Intake on Heart Disease Risk Factors in Postmenopausal Women	**Chlebowski**, Stefanick, Wagenknecht, Frid, Mossavar-Rahmani, Cain	Gen.	4	
66	Physical Activity and CVD in Women: the Role of Moderate vs. Vigorous Exercise	**Manson**, Mouton, LaCroix, Greenland, Oberman, Perri, Siscovick, Sheps, White, Casso, Wang, Stefanick	OS	4	
68	Reliability and Physiologic Correlates of the Physical Activity Questionnaire in the WHI	**Siscovick**, Cauley, Strickland, Rebar, Rodrigues, Going, Frid	CT	4	

MS ID	Title	Authors	Data Focus	Stage	Reference
80	Insulin Resistance and Weight Change in Postmenopausal Black and White Women	**Howard**, Adams-Campbell, Passaro, Black, Stevens, Wagenknecht, Rodgrigues, Safford, Allen	Gen.	4	
84	Research Staff Turnover and Participant Adherence in the WHI	**Jackson**, Chlebowski, Huber, Boe, Granek, Snetselaar, Meyer, Milas	CT	4	
91	Adherence to NCEP Lifestyle Guidelines by Hyperlipidemic Women in the OS	**Hsia**, Frishman, Rosaal, Stefanick, Howard, Snetselaar, Cochrane	OS	4	
92	Comparison of Self-report, Discharge Diagnosis, and Adjudication of Cardiovascular Events in the WHI	**Heckbert**, Hsia, Kooperberg, McTiernan, Curb, Barbour, Gaziano, Safford, Psaty, Frishman	Gen.	4	
100	Outcomes of Six Month Recall Mammography for Abnormal Findings on Screening Mammograms	**Yasmeen**, Romano, Khandekar, Robbins, Chlebowski, Lane	Gen.	4	
106	Utility of Body Mass Index (BMI) as a Proxy for Obesity Among White, Black, Asian, Native American and Hispanic Post-menopausal Women	**Going**, Chen, Tinker, Stefanick, St. Jeor, Lewis	Gen.	4	
107	Physical Activity Throughout the Life Course: The Women's Health Initiative	**Evenson**, Wilcox, Heiss, King, Daugherty, McTiernan	OS	4	
113	Prior Use of Oral Contraceptives and Fracture Risk in Menopausal Women	**Barad**, Kooperberg, Wactawski-Wende, Hendrix, Watts, Liu	Gen.	4	
18	The Relationship of Dietary Phytoestrogens Menopausal to Symptoms and Major Morbidity in Postmenopausal Women	**San Roman**, Woods, Caggiula, Judd, Brzyski, Liu, Burke, Assaf, Patterson	CT	3	
45	Socio-demographic Determinants of Folic Acid Intake	**Beresford**, Patterson, Kritchevsky, Wodarski, Vitolins	Gen.	3	
47	Is a "Too Low" Fat Diet a Marker of Health or Disease	**Gilligan**, Snetselaar, St. Jeor, Van Horn, Stefanick, Kotchen, Patterson	CT	3	
54	Current Treatment Patterns in Women with Hypercholesterolemia	**Manson**, Freed, Chae	Gen.	3	
55	The WHI Sleep Disturbance Scale: Scoring and Psychometric Evaluation	**Levine**, Shumaker, Naughton, Kaplan, Kripke, Bowen	Gen.	3	
56	Psychometric Evaluation of the Urinary Incontinence Scale	**Levine**, Shumaker, Naughton, Kaplan, Bowen	Gen.	3	
58	Influence of Race and Sunlight Exposure on Distribution of Bone Density Among Postmenopausal Women in the Southeast	**Oberman**, Burke, Hays, Hulka, Johnson, Lewis, Limacher, Schenken	Gen.	3	
75	Do Ethnic Differences in Lean and Fat Mass Contribute to Ethnic Differences in Bone Mineral Density (BMD)?	**Cauley**, Jackson, McGowan, LaCroix, Nevitt, Lewis, Ko, Margolis, Snetselaar	CT	3	

MS ID	Title	Authors	Data Focus	Stage	Reference
78	Association Between Antioxidants and BMD in an Ethnically Diverse Population of Older Women	**Wolf**, Cauley, Stone, Nevitt, Simon, Jackson, LaCroix, Lewis, Wactawski-Wende, LeBoff	Gen.	3	
81	The Prevalence of Urinary Incontinence in WHI Women	**Hendrix**, Clark, Ling, Dugan, Salmieri, Hurtado, McNeeley, Laube, McTiernan, Francis	Gen.	3	
90	Passive Smoke Exposure in Childhood and Adulthood and Prevalent Coronary Heart Disease in Women Enrolled in the WHI	**Wagenknecht**, Frishman, Wong, Ockene, Snetselaar	OS	3	
95	The Effects of Becoming a Widow on Health Behaviors and Health Status in Postmenopausal Women: The Women's Health Initiative	**Wilcox**, Evenson, Loevinger, Cochrane, Mouton, Wassertheil-Smoller	OS	3	
99	Risk Factor Clustering in the Insulin Resistance Syndrome and its Relationship to Cardiovascular Disease: Comparison of White and Black Postmenopausal Women	**Howard**, Criqui, Curb, Santoro, Wilson, Wylie-Rosett, Safford, Heber	OS	3	
102	Cardiovascular and Mortality Outcomes Related to Anti-Hypertensive Drug Therapy in the WHI	**Wassertheil-Smoller**, Margolis, Mouton, Trevisan, Oberman, Greenland, Kotchen, Psaty, Anderson, Black, Hilkert	OS	3	
118	Association Between Depressive Symptomatology and Physical Activity in Post-menopausal Women	**Rosal**, Ockene, Haan, Brunner, Mouton, Lopez, Perri, Cochrane, Matthews, Jackson	Gen.	3	
121	Quality of Life in Healthy Women and in Breast Cancer Survivors	**Haan**		3	

Stage
2= Approved
3= Writing group approved
4= Analysis proposed
5= Analysis in progress
6= Draft manuscript
7= Final manuscript submitted to P&P and PO
8= Final manuscript approved by P&P and PO
9= Submitted
10= In press/published

Table 8.2
Ancillary Studies

AS #	Title	Study's PI(s)	WHI Investigator	Initial D&A Approval	Intitial PO Approval	ID#s of Other Participating Clinics	Study Population	Sample Size	Specimens?	Funding Dates	Funding Status
123	Genetic and Ethnic Determinants of Nicotine Addiction in Postmenopausal Women	Sean P. David		no		21 needed	OS Blood, DM, HRT	30371	yes	4/01-4/-03	pending
122	Feasibility Study of Computerized Tailored Dietary Feedback	Karen Glanz, David Curb	David Curb	yes	yes	none	DM	36	no	3/10/00-9/00	funded
121	Hyperinsulinemia and Ovarian Cancer	Carrie Cottreau, Lewis Kuller	Lew Kuller	yes	yes	all	OS	206	yes	2000-20004	pending
120	Epidemiology of Cervical and Lumbar Stenosis	Molly T. Vogt	Lew Kuller	yes	yes	Pittsburgh, Arizona	OS	4000	no	12/00 - 11/04	pending
119	The Longevity Consortium	Robert D. Langer	Robert Langer	no			DM, HRT, OS		yes		pending
118	Accuracy of Food Portion Estimation Among Postmenopausal Women	Chrisitine L. Coy		yes	yes	none	DM	191	no	12/1999-4/2000	funded
117	Risk Factors for Dry Eye Syndrome in Postmenopausal Women	Kelley A. Kinney	Rebecca Jackson	yes	yes	none	OS	400	no	9/99-8/02	funded
116	National validation and quality assurance of vitamin D absorption from CaD tablets	Cedric Garland		no		none	CaD	300	yes	7/20/99-11/31/99	dropped
115	Diabetes In Postmenopausal Women	Barbara V. Howard	Barbara V. Howard	yes	yes	all	OS	93726	yes		pending
114	Effects of Hormone Replacement Therapy on Cardiac Function and Ischemia	Mary Haan	John Robbins	yes		1 other to participate, ID unknown	HRT	300	no	7/1/99-6/30/04	pending
113	Some Aspects of Mediterranean Diet in Relation to Risk of Chronic Diseases among Postmenopausal Women	Iman Hakim	Tamsen Bassford	yes	yes	none	OS	1000	yes	8/1/99 - 7/31/02	pending

AS #	Title	Study's PI(s)	WHI Investigator	Initial D&A Approval	Intitial PO Approval	ID#s of Other Participating Clinics	Study Popu-lation	Sample Size	Speci-mens?	Funding Dates	Funding Status
112	Motivators and Barriers to Exercise in Older Women	Mary Haan/Carol Parise	Mary Haan	yes	yes	none	OS	1100	no	9/1/99 - 9/30/00	pending
111	Role of Inflammation in Acute Myocardial Infarction in Women	David Brown	S. Wassertheil-Smoller	yes	yes	all	OS Blood Comp	750	yes	2/1/00 - 1/31/02	pending
110	Sex steroid hormones and risk of coronary heart disease: A nested case control study	Kathryn Rexrode/JoAnn Manson	JoAnn Manson	yes	yes	33	OS Blood Comp	700	yes	4/1/00 - 3/31/03	pending
109	Serum xenoestrogens and the risk of breast cancer	Vanessa Barnabei	Jane Kotchen	yes	yes	none	OS Blood Comp		yes	12/99 - 12/01	pending
108	Gene-environment effects and colorectal cancer	Rowan Chlebowski/Henry Lin	Rowan Chlebowski Harbor UCLA	yes	yes	all	OS Blood Comp	2000	yes	4/1/00 - 3/31/05	pending
107	Hashimoto's Thyroiditis in Postmenopausal Women	Margita Zakarija		yes	yes	51	OS Blood Comp	2900	yes	4/1/00 - 3/31/05	pending
106	Gene-Diet Interactions in Human Breast Cancer Risk	Jennifer Hu	Electra Paskett	no		none	OS Blood Comp	800	yes	6/1/99 - 5/31/03	pending
105	Xanthophyll Pigments in the Diet, Blood and Ocular Macula and Relationship to Age-Related Eye Disease in the Women's Health Initiative	Julie Mares-Perlman	Catherine Allen	yes	yes	4 others to participate, Ids unknown	OS Blood Comp	2880	yes	4/1/00 - 3/31/04	funded
104	Tamoxifen Prevention: Is it acceptable to women at risk?	John Robbins	John Robbins	yes	yes	none	OS	150	no	7/1/99 - 6/30/01	pending
103	Effects of Hormone Replacement Therapy on Cognitive Aging: Women's Health Initiative Study of Cognitive Aging (WHISCA)	Sally Shumaker		yes	yes		HRT	1800	no	4/1/99 - 3/31/05	pending

AS #	Title	Study's PI(s)	WHI Investigator	Initial D&A Approval	Intitial PO Approval	ID#s of Other Participating Clinics	Study Popu-lation	Sample Size	Speci-mens?	Funding Dates	Funding Status
102	Quality of Life Improvements and Willingness to Pay: An Investigation of Selective Estrogen Receptor Modulators	Mona Fouad	Albert Oberman		yes	none	OS	120	no	10/98 - 9/98	funded
101	Women's Health Oral History Project	Catherine (Kit) Allen	Catherine Allen	yes	yes	none	DM+HRT+OS	50	no	1/99 - 12/00	funded
100	Genetic, Biochemical and Behavioral Determinants of Obesity	Jennifer Hays	Jennifer Hays	yes	yes		OS	775	yes	4/1/99 - 3/31/01	pending
99	GENNID Study	Rowan Chlebowski		yes	yes	none	ALL	40	yes	12/1/98 - 3/31/00	funded
98	Bone mineral density as a predictor for periodontitis	Jean Wactawski-Wende		yes	N/A	none	OS	1000	yes	5/1/99 - 4/30/02	pending
97	Modeling serum markers for cost-effective ovarian cancer screening	Garnet Anderson		yes	yes	all	OS	720	yes	4/1/00 - 3/31/04	funded
95	Work organization, psychological distress, and health among minority older women	Beatriz Rodriguez		yes	N/A	none	OS	500	no	till 12/31/2000	funded
93	The Epidemiology of Venous Disease	Michael Criqui		yes	no		OS	725	no	3/11/98 - 6/30/99	funded
92	Fasting glucose in baseline plasma from all CT participants	Barbara Howard					CT		no	N/A	pending
90	Biochemical and genetic determinants of fracture in postmenopausal women	Cummings and Jamal	Charles Kooperberg	yes	yes	none	OS	910	yes	6 or 7/99 sub	pending
86	A Pilot Study to Determine the Sensitivity of Form 39 to Impaired Executive Control Function (ECF) as measured by the CLOX: an Executive Clock-Drawing Task	M.J. Polk	Robert Schenken			none	HRT	50	no	N/A	funded

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84	Apolipoprotein E genotype, ERT use, and fat-soluble vitamin intake: Effects on Cognitive Function in Older Women	Julie E. Dunn	Philip Greenland	yes	yes	none	DM+OS	260	yes	11/98 - 12/03	funded
83	Thrombotic, Inflammatory, and Genetic Markers for Coronary Heart Disease in Postmenopausal Women: A WHI Umbrella Study	Paul Ridker	JoAnn Manson	yes	yes	none	OS	1300	yes	7/1/99 - 6/30/03	funded
82	Extension of Bone Mineral Density Assessment in WHI Native American Women	Zhao Chen	Cheryl Ritenbaugh	yes	yes	none	OS	200	no	7/1/97 - 6/30/01	funded
78	Community Strategy to Retain Women Enrolled in Research	Mona Fouad		yes	N/A	none	CT	40	no	7/1/97 - 9/30/97	funded
76	Tailored Messages to Enhance Adherence of Older Women to Dietary Programs for Breast Cancer control	Rowan Chlebowski	Linda Lillington	yes	yes	none	DM	28	no	9/1/97 - 8/13/98	funded
75	Adherence to Dietary Modification in the WHI	Milagros C. Rosal	Judith Ochene	yes	N/A	6 (does not specify which CC's)	DM	480	no	9/1/97 - 8/30/02	funded
74	The Effectiveness of Individual Versus Group Behavioral Strategies to Increase Participants Adherence	Lois Wodarski	Maurizio Trevisan	yes	yes	none	DM	50	no	7/1/97 - 9/30/97	funded
73	Psychosocial and Cultural Determinants of NIDDM in Latinas	Deborah Parra-Medina	Robert Langer	yes	yes	3	OS	228	yes	5/1/97 - 4/30/98	funded
72	Ethnicity, Body Composition, Bone Density and Breast Cancer	Zhao Chen	Cheryl Ritenbaugh	yes	yes	none	OS	800	no	9/1/97 - 8/30/02	funded

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70	The Prevalence & Prognostic Importance of Myocardial Ischemia During Daily Life, & its Relationship to Migraine Status:WHI	David Sheps	David Sheffield	yes	yes	10	OS	3200	no	9/1/97 - 8/31/00	funded
68	Coronary artery calcification detected with Ultrafast CT as an indication of CAD in OS participants	Judith Hsia	Judith Hsia	yes	yes	51	OS -	782	no	1/1/97 - 12/31/05	funded
67	Prevalence and Natural History of Autoimmune Thyroid Disease is Postmenopausal Women	Marjita Zakarija	Marianna Baum	yes	N/A	51	OS Blood Comp	1040	yes	7/97 - 3/31/05	funded
65	Incidence of Benign breast disease in the DM CT - Pilot	Tom Rohan	A. McTiernan	yes	yes	all	DM	200	no	4/1/98 - 6/30/99	funded
63	Development and Evaluation of Eating Style Index	Pam Haines		yes	yes		OS	800	no	10/1/96 - 6/30/99	funded
62	Prevention of age-related maculopathy in the WHI HRT CT: WHI-SE	Mary Haan	Mary Haan	yes	no		HRT	3300	no	9 year study	funded
61	Longitudinal Assessment of Memory Functioning in the WHI Clinical Trial	Beth Ober	Mary Haan	yes	yes		HRT	110	no	6 year study	funded
60	Fat Intake in Husbands of WHI Dietary Arm Participants	James Shikany	Al Oberman	yes	yes	none	DM Partners		no	12/1/96	funded
58	Enrollment of Hispanic Women in Prevention Trials	Edward Trapido	Marianna Baum	yes	yes	none	All	120	no	9/1/96 - 8/31/99	pending
57	Hispanic Women's Advocacy and Retention Strategies	Cheryl Ritenbaugh	Cheryl Ritenbaugh	yes	yes	none	OS	120	no	9/1/96 - 8/31/98	funded
56	Behavioral and psychosocial predictors of dietary change in postmenopausal women	Joan Pleuss	Alice Thomson	yes	yes	none	DM	260	no	9/1/96 - 8/31/98	funded
52	Endogenous Sex Hormones and Breast Cancer in Older Women	Anne McTiernan	A. McTiernan	yes	yes	All	OS	782	yes	7/1/99 - 6/30/04	pending

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50	Nutrition Practice Guidelines for Maintaining Low-Fat Dietary Change in Post Menopausal Women	Beth Burrows	Ross Prentice	yes	yes	none	DM	200	no	10/1/96 - 9/30/97	funded
48	Prostate Ca Survey of Spouses of WHI Screened Women	Sylvia Smoller	Sylvia Smoller	yes	yes	none	All	1607	no	2/1/96 - 6/30/96	funded
47	Effect of diet intervention on motivation to make other health-related changes	Langer/Lo	Robert Langer	yes	yes	none	DM	150	no	5/1/96 - 4/30/97	funded
44	Estrogen and Vaginal pH	Anthony Schaeffer	Philip Greenland	yes	N/A	none	HRT	100	yes	4/1/96 - 3/31/01	funded
40	Ethnic and age differences in use of Mammography	S. Wassertheil-Smoller	S. Wassertheil-Smoller	yes	yes	none	All	All	no	N/A	funded
39	The Effects of HRT on the Development and Progression of Dementia	Sally Shumaker	Curt Furberg	yes	yes	all except #18	HRT	4800	no	5/1/96 - 4/30/02	funded
36	Hormone Replacement Therapy and Changes in Mammographic Density	Barbara Hulka	A. McTiernan	yes	yes	ALL	HRT	NA	no	1/98 - 12/07	funded
34	Ethnic Differences in Hip Bone Geometry by DXA and QCT	Dorothy Nelson	Susan Hendrix	yes	yes	none	HRT	330	no	12/1/96 - 12/31/02	funded
33	The Association of HRT with Abdominal and Total Body Fat in Postmenopausal Women	Charlotte Mayo	Al Oberman	yes	yes	none	OS	690	no	7/31/95 - 3/31/96	funded
31	Eye Care Use	Robert Kleinstein	Al Oberman	yes	yes	none	OS	300	no	N/A	funded
28	Perspectives on Aging	S. Wassertheil-Smoller	S. Wassertheil-Smoller	yes	yes	none	OS	NA	no	5 year follow-up	pending
25	Ankle-Arm Blood Pressure Index Measurement	Kamal Masaki	David Curb	yes	yes	none	OS	2700	no	2/96 - 1/98	funded

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24	Cross-ethnic Comparisons of Skeletal Health of Postmenopausal Women in San Diego County	Diane Schneider	Robert Langer	yes	yes	none	OS	168	no	1/3/95 - 1/2/97	funded
17	Domestic Violence in Older Women	Charles Mouton	Norm Lasser	yes	yes	none	OS	1000	no	10/25/94 - 10/24/96	funded
15	The Relationship between Osteopenia and Periodontitis	Jean Wactawski-Wende	Maurizio Trevisan	yes	yes	none	OS	1300	no	9/16/96 - 9/15/00	funded
14	High Density Lipoprotein Metabolism	Scott Going, Tamsen Bassford	Tom Moon	yes	N/A	none	OS	200	no	7/1/94 - 6/30/96	funded
13	Prevalence and Correlates of Lumbar Spinal Stenosis	Lewis Kuller	Lew Kuller	yes	N/A	none	CT	150	no	12 year study	funded
11	Validation and Exploration of Sleep and Mood Predictors	Daniel Kripke	Robert Langer	yes	N/A	none	OS	600	yes	8/1/95 - 7/31/99	funded
9	An investigation of oral hard tissue status in relation to skeletal bone mineral density measures and osteoporosis	Marjorie Jeffcoat	Al Oberman	yes	N/A	none	OS	650	no	6/1/95 - 5/31/02	funded