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Foreword

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INTRODUCTION

With an enrollment of 161,809 participants at 40 clinical centers, the Women's Health Initiative (WHI) is the largest and most comprehensive set of women's health studies ever conducted. Scientifically, the WHI is supported by a long history of developmental work, including epidemiologic and animal studies, and feasibility and intermediate endpoint trials in key areas of women's health. Societally, the existence of this program is testament to the powerful interest in and need for definitive research in the health concerns of postmenopausal women.

The history and rationale for the WHI have been described previously (1,2). National Institutes of Health (NIH) Director Bernadine Healy initiated the program in 1991 and obtained funding from Congress beginning in 1992. A multi-institute planning group of NIH scientists evaluated the most pressing health needs of older women, considered the most promising interventions to be tested, and developed the framework for the study. At critical junctures, input was sought from non-NIH scientists and from the public. For design purposes, the planning group identified cardiovascular disease, breast and colorectal cancer, and osteoporotic fractures as the primary outcomes of interest. However, it was decided that the planned studies should not focus narrowly on these outcomes, but should assess the impact of the prevention therapies on overall health. The study plan was developed into requests for contract proposals for the Clinical Coordinating Center and the Clinical Centers. The Clinical Coordinating Center was funded in the fall of 1992, and the first set of 16 clinical centers was funded in the spring of the following year. The Clinical Coordinating Center investigators drafted the first version of the protocol, which was subsequently refined by investigators from the Clinical Centers. In early 1993, the investigators drafted the first elements of the Manual of Operating Procedures, and by the fall of 1993 enrollment of participants had begun. Recruitment and clinic visit procedures were refined based on the early experience in the first set of Clinical Centers and prior to the engagement of the second set of 24 clinical centers in 1995. Recruitment goals having been met, enrollment ended in 1998.

At its inception, the WHI was administered from the Office of the Director at the NIH. This unusual situation came about because of the Director's interest in the study and because the aims of the program cut across boundaries within the NIH. However, by 1997 the program had been well established and it became clear that the National Heart, Lung, and Blood Institute (NHLBI) would be a more appropriate home for this research program. Accordingly, the program was moved to the Office of the Director at the NHLBI, while maintaining the links with staff from other NIH institutes.

This report highlights the achievement of the recruitment goals. In fact, the original goal of 57,000 participants for the WHI Clinical Trial was increased to 67,000 because of a significant protocol modification (see the article in this issue entitled "WHI Postmenopausal Hormone Trials") together with experience that relatively few women were enrolling in both the dietary and hormone trials. The new goal was exceeded with a final enrollment of 68,133 participants in the Clinical Trial. The original estimate was that 100,000 women initially screened for the Clinical Trial would enter the WHI Observational Study. Early experience indicated that the Observational Study would become oversubscribed rapidly, at some cost to Clinical Trial enrollment. Thus, enrollment targets for the Observational Study were scaled back for much of the recruitment period and were increased again in the final months once it was clear that the Clinical Trial target would be met. Enrollment into the Observational Study was stopped at 93,676 so that the study could turn its attention to the next priority: adherence, retention, and outcomes ascertainment in the Clinical Trial. The fulfillment of recruitment goals was possible because of the strong commitment of many investigators and staff, and the willingness of so many women to offer their time, experience, and energy to this endeavor.

As important as overall recruitment goals were, it was equally important that women from minority groups were adequately represented in the study population. Efforts were made to assure that meaningful numbers of Black, Hispanic, Asian/Pacific Islander and American Indian women were enrolled in the WHI. The final numbers reflect minority representations close to or at the proportions found in the U.S. population of women in the age range studied. This promotes the generalizability of the findings,

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and allows for informative subgroup analyses. In the Clinical Trial, the statistical power for the primary outcomes is predicated on the size of the entire cohort, but various prespecified subgroup analyses will be performed to examine the consistency of findings across subgroups. For intermediate outcomes, including blood biomarkers, the minority subgroups are oversampled to improve the statistical power to measure the impact of the study treatments on risk markers. Because of the large numbers in the Observational Study, there will be ample opportunity to perform within-group analyses examining the relationship of risk factors to important clinical outcomes such as heart disease, breast and colorectal cancer, and osteoporotic fractures. To the best of our knowledge, the WHI is not only the largest and most comprehensive study of women to date, it is also the largest and most comprehensive study of minority women.

The primary objective of this issue is to describe the baseline characteristics of participants in the WHI Clinical Trial and Observational Study. The secondary objectives are to document methods that are critical to understanding study findings and to provide guidance and insight from the WHI experience to investigators and funding agencies embarking on similar large multicenter studies. Separate articles are devoted to the Clinical Trial components testing three prevention strategies: postmenopausal hormones, low-fat dietary modification, and calcium/vitamin D supplementation. Another article is devoted to the large Observational Study. These descriptions of the methods and baseline characteristics of participants are introduced by articles on recruitment strategies and on the implementation of the study design, including data management and quality assurance procedures. Finally, there is a description of the methodology used for ascertaining and classifying clinical outcomes. This issue does not describe the WHI Community Prevention Study, which will be reported elsewhere.

The data presented herein include: (1) data obtained from WHI participants during the screening and enrollment process; (2) laboratory results obtained from specimens collected during screening and subsequently analyzed; and (3) limited year 1 data to address methodologic issues in the screening data (see Ritenbaugh's article in this issue entitled "WHI Dietary Modification Trial"). Simple descriptive statistics are provided to document the observed distributions. No adjustments for age, race, or other factors were incorporated, though many of the displays provide tabulations by these important design factors. Each article presents the baseline data critical for understanding how that study component is positioned to address the targeted hypotheses. Comparisons across study components are not considered inherently meaningful because of the separate eligibility requirements; however, an extensive display of the information by race and ethnicity for the Clinical Trial and Observational Study is provided (see the appendix to Hays' article entitled "Recruitment Methods and Results"). The WHI Observational Study baseline dataset will be available at http://www.nhlbi.nih.gov/resources/index.htm in December 2003.

What about the future of WHI? Four years after the end of recruitment, the investigators and staff are fully engaged with meeting the challenges of adherence, retention, and outcomes. Laboratory analyses of risk markers are well underway, and analyses of the major trial outcomes are routinely conducted and reported to an independent data and safety monitoring board. The database on exposures and outcomes already allows WHI investigators to rapidly and more completely examine issues that have been raised by smaller studies. The parallel conduct of the Clinical Trial and Observational Study will make WHI an important laboratory for examining the strengths and weakness of observational studies in evaluating potential intervention strategies.

Several ancillary studies are underway or are being planned. The largest ancillary study is the WHI Memory Study, which examines the effect of postmenopausal hormones on the incidence and progression of dementia, including Alzheimer's disease. A second large ancillary study will examine the effects of hormone use on macular degeneration. Other ancillary studies in various stages of development will use the blood and DNA resource in the Observational Study together with questionnaire data to refine information about known risk factors, and to discover new risk factors for the more important diseases of postmenopausal women.

Of course, the major contribution of the WHI lies somewhat further in the future, when the trials are completed. At that time, definitive answers will be given to questions that have vexed the medical profession and the public alike. For example, is long-term hormone use beneficial? Will a low-fat eating pattern prevent cancer? And how effective is calcium and vitamin D for preventing fractures? Finally, will these commonly promoted but unproven prevention treatments have an effect on overall health and well-being? The investigators and participants in this unique venture are hopeful that the answers will benefit the daughters and granddaughters of the trial participants, as well as the current generation of women who are in the postmenopausal stage of life.

APPENDIX: ACKNOWLEDGMENTS

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Implementation of the Women's Health Initiative Study Design

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WHI CLINICAL TRIAL AND OBSERVATIONAL STUDY

The Women's Health Initiative (WHI) Clinical Trial (CT) includes three overlapping components, each a randomized controlled comparison among women who were postmenopausal and 50 to 79 years of age at randomization. The dietary modification (DM) component randomly assigned 48,836 (target 48,000) eligible women to either a sustained low-fat eating pattern (40%) or self-selected dietary behavior (60%), with breast cancer and colorectal cancer as designated primary outcomes and coronary heart disease as a secondary outcome. The nutrition goals for women assigned to the DM intervention group have been to reduce total dietary fat to 20%, and saturated fat to less than 7% of daily calories and, secondarily, to increase daily servings of vegetables and fruits to at least five and of grain products to at least six and to maintain these changes throughout trial follow-up. The randomization of 40%, rather than 50%, of participating women to the DM intervention group was intended to reduce trial costs, while testing trial hypotheses with specified power.

The postmenopausal hormone therapy (PHT) component comprises two randomized, double-blind trials among 27,347 (target 27,500) women, with coronary heart disease (CHD) as the primary outcome, with hip and other fractures as secondary outcomes, and with breast cancer as a potential adverse outcome. Of these, 10,739 (39.3% of total) were post-hysterectomy at randomization, in which case there was a 1:1 randomized double-blind allocation between conjugated equine estrogen (E-alone) 0.625 mg/day or placebo. The remaining 16,608 (60.7%) of women, who had a uterus at baseline, were randomized 1:1 to the same preparation of estrogen plus continuous 2.5 mg/day of medroxyprogesterone (E + P) or placebo. These numbers compare with design goals of 12,375 for the unopposed estrogen comparison, and 15,125 for the E + P comparison, based on an assumption that 45% of women would be post-hysterectomy. A total of 8,050 women (29.4% of the PHT program enrollment) were randomized to both the DM and PHT components.

At their one year anniversary from DM and/or PHT trial enrollment all women were further screened for possible randomization in the calcium and vitamin D (CaD) component, a randomized double-blind trial of 1000 mg elemental calcium plus 400 international units of vitamin D_3 daily, vs. placebo. Hip fracture is the designated primary outcome for the CaD component, with other fractures and colorectal cancer as secondary outcomes. A total of 36,282 (53.3% of clinical trial enrollees) were randomized to the CaD component. While the WHI design estimated that about 45,000 women would enroll in the CaD trial component, protocol planning activities also included projected sample sizes of 35,000 and 40,000 and noted that most WHI objectives could be met with these smaller sample sizes.

The total clinical trial sample size of 68,133 is only 60.7% of the sum of the individual sample sizes for the three clinical trial components, providing a cost and logistics justification for the use of a partial factorial design with overlapping components.

Age distribution goals were specified separately for the DM and PHT trials as follows: 10%, ages 50 to 54 years;

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Selected Abbreviations and Acronyms

CaD = calcium and vitamin D
CC = clinical center
CCC = Clinical Coordinating Center
CHD = coronary heart disease
CT = clinical trial
DM = dietary modification
DSMB = Data and Safety Monitoring Board
ECG = electrocardiogram
E-alone = (unopposed) estrogen trial
E+P = estrogen plus progestin trial
FFQ = food frequency questionnaire
NHLBI = National Heart Lung and Blood Institute
NIH = National Institutes of Health
OBF = O'Brien-Fleming
OS = observational study
PHT = postmenopausal hormone therapy
PMC = performance monitoring committee
QA = quality assurance
WAN = wide area network
WHI = Women's Health Initiative

20%, ages 55 to 59 years; 45%, ages 60 to 69 years; and 25%, ages 70 to 79 years. While there was substantial interest in assessing the benefits and risks of each trial intervention over the entire 50- to 79-year age range, there was also interest in having a sufficient representation of younger (50 to 54 years) postmenopausal women for meaningful age group-specific intermediate outcome (biomarker) studies. Sufficient numbers of older (70 to 79 years) women allowed for studies of treatment effects on quality of life measures, including aspects of physical and cognitive function. Differing age incidence rates within the 50 to 79 years age range, and across the outcomes that were hypothesized to be affected by the interventions under study provided additional motivation for a prescribed age-at-enrollment distribution. Age distribution goals were not specified for the observational study (OS) or CaD.

The enrollment of such a large number of women, meeting designated eligibility and exclusionary criteria [see (1) and Hays' article in this issue] proved to be a challenge, particularly for the hormone component, since many women who volunteered for WHI were already taking postmenopausal hormones and did not wish to be randomized to take hormones or placebo, while other women had already made a decision against their use. Recruitment goals were increased to account for the fact that only 40 clinical centers were selected for participation, as compared with a planned 45. These issues led to some prolongation of the recruitment period and to a reduction in average follow-up in the CT to about 8.5 years, as compared with the target 9 years.

Women who were screened for the clinical trial but proved to be ineligible or unwilling to be randomized were offered the opportunity to enroll in the OS. The OS was intended to provide additional knowledge about risk factors for a range of diseases, including cancer, cardiovascular disease, and fractures. It has an emphasis on biological markers of disease risk, and on risk factor changes as modifiers of risk.

Hays' article in this issue provides further information on eligibility and exclusionary criteria for the various components of the WHI program, and provides descriptive information on the recruited cohorts.

Study Organization

In addition to the clinical centers, the study is implemented through a Clinical Coordinating Center (CCC) located in Seattle with various collaborators providing specific expertise, as described below. The National Heart, Lung, and Blood Institute (NHLBI) sponsors the program with input from the National Cancer Institute, the National Institute of Aging, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the NIH Office of Research on Women's Health, and the NIH Director's office. The directors of participating NIH institutes and offices form a consortium that advises the NHLBI Director concerning the WHI, as needed. A special working group of the National Heart, Lung, and Blood Council also advises the NHLBI Director concerning the WHI.

A Steering Committee, consisting of the Principal Investigators of the 40 clinical centers, and CCC and NHLBI representatives, is responsible for major scientific and operational decisions. An Executive Committee identifies, prioritizes, and coordinates items for Steering Committee discussion. Program activities are implemented through a regional organization that categorizes clinical centers geographically (West, Midwest, Northeast, and Southeast). Principal Investigators and staff groups defined by project responsibilities (clinic manager, clinic practitioner, nutritionist, recruitment coordinator, data coordinator, outcomes coordinator) meet regularly by conference call within regions to discuss implementation plans and issues. Regional staff group representatives also confer regularly to ensure national coordination. Nine advisory committees (behavior, calcium and vitamin D, design and analysis, dietary modification, post-menopausal hormone therapy, morbidity and mortality, observational study, publications and presentations, special populations) composed of study investigators having expertise in the major substantive areas provide recommendations to the Steering Committee on relevant issues as they arise. The CCC participates and provides liaison support in these various contexts. Figure 1 shows the WHI governance, including NIH advisory committees.

Principal Clinical Trial Comparisons, Updated Power Calculations, and Safety and Data Monitoring

This section provides sample sizes by age for each clinical trial component and for the OS, and provides power calculations for key outcomes for each trial component. Relative to

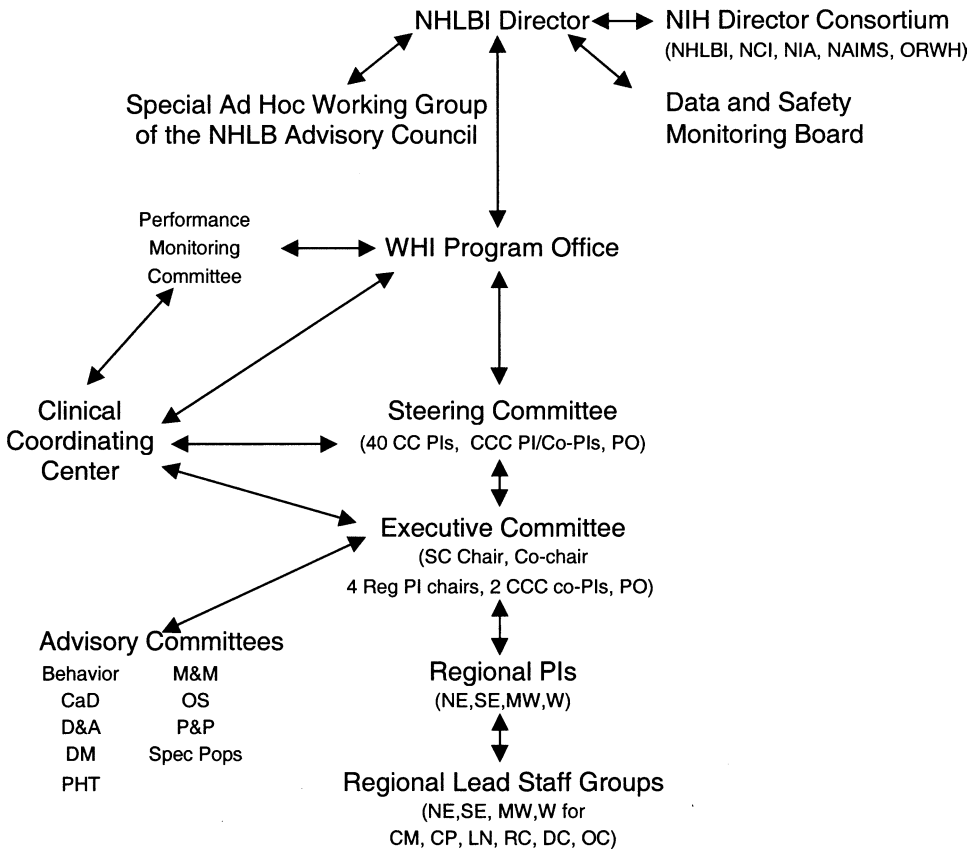

FIGURE 1. WHI Study governance.

the basic WHI design manuscript (1), these calculations have been updated to reflect the sample size and age distribution achieved and the projected average follow-up duration.

The target sample sizes were based on consideration of the probability of rejecting the null hypothesis of no treatment effect (i.e., power) on the designated primary outcome under a set of design specifications, including age-specific control group primary outcome incidence rates, intervention effects on incidence rates as a function of time from randomization, intervention adherence rates, and competing risk mortality rates. These assumptions have previously been listed in (1) where an extensive bibliography is cited to provide the rationale for these assumptions.

The power calculations were based on so-called weighted logrank statistics that accumulate the differences between the observed numbers of primary outcome events in the intervention group and the expected number of such events under the null hypothesis across the follow-up period. Early events, which may be less likely to be affected by intervention activities, are downweighted relative to later events. Specifically, the observed minus expected differences are weighted linearly from zero at randomization to a maximum value of one at a certain time from randomization and are constant (at one) thereafter. For cardiovascular disease and fracture incidence, this 'certain time' was taken to be 3 years, whereas for cancer and mortality it was taken to be 10 years. For coronary heart disease incidence, the event times are grouped into 3-year follow-up periods, to accommodate the inclusion of silent myocardial infarctions detected by routine electrocardiograms, which are to be obtained at baseline and every 3 years during follow-up for clinical trial participants. A weighted odds ratio test statistic is then used to acknowledge this grouping. Detail on related power calculations and statistical model can be found in Lakatos (2) and Self et al (3).

Table 1 shows the number of enrollees, and percentages of the total, by age category for each component of the CT and the OS.

Table 2 shows the projected power; that is, the probability of rejecting the null hypothesis, for the key outcomes for each clinical trial comparison, taking account of the age-specific sample sizes in Table 1. Projected power is given both at planned termination in mid-2005, in which case the average follow-up duration will be about 8.5 years in the DM and hormone components and about 7.5 years in the CaD component, as well as 3 years earlier in mid-2002. The intervention effects shown in Table 2 represent the projected effect size after accounting for a certain degree of non-adherence and loss to competing risks. Comparison with projected power calculations at the design stage (1)

TABLE 1. Women's Health Initiative sample sizes (% of Total) by age group

Age group	Dietary Modification	Postmenopausal hormones		Calcium and Vitamin D	Observational Study
		E-alone	E + P		
50–54	6961 (14)	1396 (13)	2029 (12)	5157 (14)	12,386 (13)
55–59	11,042 (23)	1914 (18)	3439 (21)	8265 (23)	17,319 (18)
60–69	22,713 (47)	4852 (45)	7510 (45)	16,520 (46)	41,197 (44)
70–79	8120 (17)	2577 (24)	3576 (22)	6340 (17)	22,774 (24)
Total	48,836	10,739	16,608	36,282	93,676

indicates that the somewhat prolonged recruitment period and the minor departures from target in sample sizes by age category had little effect on projected study power. The CHD and hip fracture power projections for the estrogen vs. placebo comparison is somewhat reduced by a smaller than targeted sample size (10,739 vs. 12,375) in this clinical trial component.

It is also of interest to consider projected power for active hormones vs. placebo, combining the two hormone preparation comparisons. With the achieved sample sizes and projected follow-up durations the combined power at planned termination is 98% for CHD, 91% for hip fractures, greater than 99% for combined fractures, and 74% for breast cancer (98% with an additional 5 years of follow-up). Power calculations for representative comparisons in the OS have been given previously (1).

An independent Data and Safety Monitoring Board (DSMB) is charged with monitoring the clinical trial to ensure participant safety, to assess conformity to program goals, and to examine whether there is a need for early stoppage or other modification of any trial component. The DSMB is composed of senior researchers, otherwise not associated with the study, who have expertise in relevant areas of medicine, epidemiology, biostatistics, clinical trials, and ethics. The DSMB meets semi-annually to review study progress, including its status in the context of emerging external data. The board provides recommendations to the NHLBI Director (see Figure 1). The DSMB reviewed and approved the protocol and consent forms prior to study implementation and they advise NHLBI on any significant protocol changes.

Throughout the period of study conduct, the DSMB reviews data on recruitment, adherence, retention, and outcomes. The DSMB is the only group given access to treatment arm comparisons outside of the necessary CCC and NHLBI staff. As such, they determine whether the

TABLE 2. Updated statistical power for each component for the Clinical Trial

Outcome	Disease probability (%) (×100)[1]		Intervention effect[2] (%)	Early termination (2002)		Planned termination (2005)	
	Control	Intervention		Avg. follow-up duration (years)	Projected power (%)	Avg. follow-up duration (years)	Projected power (%)
Dietary Modification component (n = 48,836)							
*Breast cancer	2.72	2.35	14	5.5	37	8.5	84
*Colorectal cancer	1.39	1.12	19	5.5	35	8.5	87
CHD	3.78	3.27	14	5.5	61	8.5	84
Postmenopausal hormones–E-alone (n = 10,739)							
*CHD	4.63	3.67	21	5.5	49	8.5	72
Hip fracture	2.86	2.25	21	5.5	34	8.5	55
Combined fracture[3]	11.02	8.81	20	5.5	85	8.5	97
Breast cancer[4]	4.38	5.36	(22)	8.5	37	13.5	71
Postmenopausal hormones–E + P (n = 16,608)							
*CHD	4.45	3.52	21	5.5	66	8.5	87
Hip fracture	2.74	2.16	21	5.5	47	8.5	72
Combined fracture[3]	10.80	8.63	20	5.5	96	8.5	>99
Breast cancer[4]	4.37	5.34	(22)	8.5	52	13.5	88
Calcium and Vitamin D (n = 36,282)							
*Hip fracture	2.23	1.77	21	4.5	58	7.5	88
Combined fracture[3]	8.93	7.23	19	4.5	99	7.5	>99
Colorectal cancer	1.25	1.02	18	4.5	20	7.5	66

*Indicates primary outcome.
[1]Cumulative disease probability to planned termination (×100).
[2]One minus ratio of control to intervention cumulative incidence rates at study termination (×100).
[3]Includes proximal femur, distal forearm, proximal humerus, pelvis, and vertebra.
[4]An additional five years of follow-up is planned in the hormone trials for monitoring breast cancer incidence. Intervention effects in parentheses denote a projected adverse effect.

existing data demonstrate either significant or unanticipated risk or unexpectedly strong benefits, in which case early trial termination, or modification, may be recommended. A particular complexity in this study, as often exists in prevention studies, is the need to consider effects on multiple disease processes that may differ in direction, timing, and magnitude.

In the WHI, trial monitoring for consideration of early stopping is based on the following principles and procedures:

- Each trial component (DM, PHT, and CaD) is evaluated separately, so that a stopping decision for one will not necessarily impact the continuation of the other two.
- The evaluation of each intervention includes an assessment of the overall intervention effects on health through use of a global index. This global index is defined as time to first incident event where the events included were selected based on a priori evidence for each intervention as shown in Table 3.
- Early stopping for benefit would be considered if the primary endpoint comparison crossed a 0.05 level O'Brien-Fleming (OBF) boundary and the global index provided supportive evidence defined by crossing the 0.1 level OBF boundary in favor of the intervention. For the DM, a Bonferroni correction is used to acknowledge the fact that there are two designated primary endpoints. This correction allows a stopping recommendation to be made if the boundary is crossed for either of the primary endpoints, without exceeding the designated probability (0.05) of falsely rejecting the overall null hypothesis.
- Early stopping for adverse effects uses a two-step procedure with a 0.1 level OBF boundary for primary safety endpoints, a Bonferroni-corrected 0.1 level OBF boundary for all other safety endpoints, and a lower boundary of $z = -1.0$ for the global index to signify supportive evidence for overall harm.

TABLE 3. Trial monitoring endpoints for the WHI Clinical Trial components (based on assessment of overall intervention effects using a global index)

	DM	PHT	CaD
Primary endpoint(s)	Breast cancer, colorectal cancer	CHD	Hip fractures
Primary safety endpoint	N/A	Breast cancer	N/A
Other endpoints included in global index	CHD, death from other causes	Stroke, pulmonary embolism, hip fractures, colorectal cancer, endometrial cancer (E + P trial only), death from other causes	Colorectal cancer, breast cancer, other fractures, death from other causes

Weighted logrank test statistics are used to test the difference between intervention and control event rates for each outcome. These weights were specified to yield efficient test statistics for the primary outcome under trial design assumptions. As such, these tests need not be sensitive to unexpected effects, whether adverse or beneficial, on any of the study outcomes. Consequently, the DSMB also informally examines unweighted logrank statistics, as well as weighted and unweighted tests for various intervals of time since randomization and for selected subgroups of participants (e.g., specific age groups), toward ensuring participant safety. Some further detail on clinical trial monitoring methods and their rationale is given in (4).

Clinical trial monitoring reports prepared on a semiannual basis throughout trial follow-up also present data on the adherence to intervention goals, the rates of participation in follow-up and other program activities, and control group incidence rates. These data are used to develop updated power calculations, along the lines of Table 2, to help assess conformity to overall design goals, and to alert the DSMB to emerging problems. Data on selected biomarkers and intermediate outcomes are also assembled, as such data can provide an objective assessment of the extent to which intervention goals are achieved, and can provide insights into processes that can explain intervention effects on disease outcomes.

BIOMARKERS, INTERMEDIATE OUTCOMES, AND ADDITIONAL CT/OS ANALYSES

Beyond testing primary and secondary hypotheses, the clinical trial is designed to support specialized analyses to explain treatment effects in terms of intermediate outcomes, and both the CT and OS are designed to produce new information on risk factors for cardiovascular disease, cancers and other diseases. With appropriate informed consent, the basic WHI program stores serum and plasma from participants at baseline, and at selected follow-up times (1 year from enrollment in the CT and 3 years from enrollment in the OS). In addition, white blood cells ("buffy coats") are stored from CT and OS participants at baseline. These blood specimens are used for specialized studies related to participant safety and CT intervention adherence, and for externally funded ancillary studies. Stored blood components collected from each participant during screening include 7.2 ml serum (in 4×1.8 ml vials), 5.4 ml citrated plasma (in 3×1.8 ml vials), 5.4 ml EDTA plasma (in 3×1.8 ml vials), and two aliquots of buffy coat.

A 6% subsample of clinical trial participants, randomly selected at baseline, provides blood specimens at 3, 6, and 9 years following randomization. Several biomarkers in the

AEP Vol. 13, No. S9
October 2003: S5–S17

6% CT subsample will be measured to assess intervention adherence and intermediate effects of the trial interventions. These include fasting lipid subfractions (total cholesterol, LDL-C, HDL-C, HDL-2, HDL-3, triglycerides, LPa), glucose, insulin, fibrinogen, Factor VIIC, Factor VII Antigen Activity, and several nutritional biomarkers (α-tocopherol, γ-tocopherol, α-carotene, β-carotene, β-cryptoxanthine, lycopene, lutein plus zeaxanthin, and retinol). A smaller fraction of women have additional biomarker measurements specific to their intervention, including hemostatic markers and more detailed hormonal and dietary analytes. To maximize data from each racial/ethnic group, as well as from each component of the trial (DM, PHT, and CaD), the sampling rates were tailored to be higher among minority women (odds for selection are at least 6-fold higher than for Caucasian women) and higher among PHT participants (8.6% sampling rate) than among DM women (4.3%). Table 4 shows the number of women in this 6% sample by study component and by racial/ethnic group. All clinical trial participants have measurement of hematocrit, white blood cell count, and platelet count at baseline.

Intermediate outcome data collected in the clinical trial include electrocardiograms (obtained as baseline, 3, 6, and 9 years among all trial participants) to ascertain "silent" myocardial infarctions and other cardiac diagnoses, and bilateral mammograms (obtained annually for PHT women and biennially for other trial participants). In the DM component, all participants complete a follow-up food frequency questionnaire at 1 year; 30% at year two, and 33% at years three and beyond so that each woman is scheduled to complete a food frequency questionnaire (FFQ) every 3 years after year two. A 4.3% subcohort of DM women, randomly selected at baseline, provide 4-day food records at 1 year and 24-hour dietary recalls at 3, 6, and 9 years; an additional independent 1% sample completes 24-hour dietary recalls during each follow-up year. In the E + P trial, all participants with a uterus have a baseline pelvic exam and endometrial aspiration; follow-up pelvic exams are performed annually with a Pap smear every 3 years either through the clinical center or the participant's personal physician. A five to six percent random sample of E + P trial participants have follow-up endometrial aspirations in years 3, 6, and 9 to ascertain endometrial hyperplasia or other pathology; a transvaginal ultrasound is performed if an endometrial aspiration cannot be obtained. In addition, all hormone component women 65 years of age and older have cognitive function assessment, and a 25% sample have functional assessment, at baseline and follow-up. A sample of women in both the CT and OS (who are enrolled at three specified clinical centers: Birmingham, Pittsburgh, and Tucson/Phoenix) have dual X-ray absorptiometry at baseline and follow-up years 1 (CT only), 3, 6, and 9 to measure change in bone mass in the hip and spine. These women also provide urine specimens, which are stored for studies of the interventions' effects on bone metabolites.

TABLE 4. Ethnicity of participants with stored blood in each component of the '6%' Clinical Trial subsample

	DM		PHT		CaD	
	N	%	N	%	N	%
American Indian/Alaska Native	76	2.7	64	2.4	56	2.4
Asian/Pacific Islander	197	7.0	176	6.5	170	7.3
Black/African American	807	28.6	696	25.8	580	24.7
Hispanic	317	11.2	411	15.8	304	13.0
White	1,375	48.7	1,296	48.0	1,195	51.0
Unknown	52	1.8	57	2.1	39	1.7
Total	2,824		2,700		2,344	

OS participants have a baseline and 3-year clinic visit to collect exposure data, physical measurements, and blood specimens (see Langer's article in this issue for descriptions). OS participants also have measurements of hematocrit, white blood cell count, and platelet count at baseline and year 3. Their exposure data and medical histories are updated annually through mailed questionnaires. A 1% sample of OS participants return to the clinic between 1 and 3 months after their baseline visit to participate in a measurement precision (reliability) substudy, at which time blood is redrawn and several selected exposure and physical measurements that are prone to measurement error are repeated. Several blood biomarkers (lipids, glucose, insulin, fibrinogen, nutrients, and other biomarkers described above for the clinical trial) are also measured in this substudy.

Analyses to explain trial intervention effects and CT/OS analyses to elucidate disease risk factors will generally take place in a case-control or case-cohort fashion to limit the number of specialized analyte determinations. Extensive self-report questionnaire data at baseline and selected follow-up times are also available for use in these analyses, and can be used to inform the case-control sampling procedure.

Data Management and Computing Infrastructure

The size and scope of the WHI creates a large and rather complex data processing load. Each clinical site has recruited at least 3000 participants, creating a local data management load as large as that for many multi-center trial coordinating centers.

The data collected for WHI fall roughly into three categories: self-report, clinical measurements, and outcomes data. Self-reported information includes demographic, medical history, diet, reproductive history, family history, and psychosocial and behavioral factors. For these areas, standardized questionnaires were developed from instruments used in other studies of similar populations. Use of medications and dietary supplements is captured directly from pill

bottles that participants bring to the clinic. To capture details of hormone use prior to WHI enrollment, an in-person interview was conducted with each woman to determine her entire history of postmenopausal hormone use. For additional diet information, four-day food records and 24-hour recall of diet were obtained from a subsample of women as described above. Dietary records were completed by the participant, reviewed and documented by certified clinic staff; a subsample was sent to the CCC for nutrient coding and analysis. The 24-hour recalls of diet were obtained by telephone contact from the coordinating center and these data were coded using the same methods as for the dietary records.

Clinical measures such as anthropometrics, blood pressure, functional status, and results from gynecologic exams are obtained by certified WHI clinic staff using standardized procedures and data collection forms and key-entered into the local study database. Limited blood specimen analyses were conducted locally and recorded. The remaining blood specimens were sent to a central blood repository where they are housed until the appropriate subsamples are identified and sent to the central laboratory for the selected analyses. Electrocardiogram and bone densitometry data are submitted electronically to respective central reading and coordination facilities. The Foreword provides the Principal Investigator name and location for these various CCC subcontractors. Additional details on data collection and analysis are provided in the appendix to this article.

Information on significant health outcomes is initially obtained by self-report. If the type of event is of interest for WHI research, additional documentation is obtained from local health care providers and a clinic physician uses this information to classify and code the event. Further details of this process may be found in Curb's article in this issue.

Data quality assurance mechanisms are incorporated at several levels, in addition to the overall quality assurance program described below. Data entry screens incorporate range and validity checks, and scanning software rejects forms containing critical errors. Routine audits of randomly selected charts document errors and provide feedback to clinical center and CCC staff. Additional data quality checks are used in creating analytic data sets. Multiple versions of most forms have been used so some data items require mapping across versions.

To support the large requirement of local operations as well as central analyses and reporting, the CCC developed and implemented a standardized computing and database management system that serves each clinical center site and the coordinating center. This computing system can be logically divided into three major areas: computing at the clinical centers; computing at the CCC; and a private wide area network (WAN). The study-wide database uses this infrastructure to provide the appropriate data management tools to all sites.

Each clinical center is equipped with its own local area network consisting of a file server, ethernet switch, 10 to 20 workstations, two or more printers, a mark sense form reader, bar code readers and a router. The router provides connectivity back to the CCC over the WAN. In some cases, the router also provides connectivity to the parent institution. The file server is configured with Windows NT Advance Server and runs its own instance of the study's Oracle database. The server also provides standardized office applications (Microsoft Office) and e-mail (Microsoft Exchange Web client). The workstations are Windows 98 clients.

The CCC maintains a cadre of application servers dedicated to the development, testing, and warehousing of the consolidated database, currently requiring 100 gigabytes. The CCC also maintains several other servers dedicated to statistical analysis, administrative support for CCC staff, website and e-mail services for study-wide communication, and centralized automated back-up for all study servers. The website and e-mail system dedicated to WHI staff and investigators is critical to study communications. With nearly 1,500 WHI staff members and investigators spread across the country including five time-zones, study-wide communication is an ongoing challenge. The website provides a kind of electronic glue for bringing together disparate groups. Investigators and staff access their e-mail through the website either over the WAN or through the Internet.

The WHI WAN is a private network, which connects clinical centers to the CCC using a combination of 56k and T1 frame-relay circuits. The WAN enables the CCC to conduct nightly backups of clinical center file servers. It also facilitates remote management and troubleshooting of clinical center equipment. In addition, it provides clinical centers direct access to the WHI e-mail system and website.

The WHI database management system is a distributed replicated database, implemented in Oracle 8.0 for Windows NT. Database design and table structure are identical across clinical centers but are populated only with data specific to that site. The average clinical center database currently requires approximately 15 gigabytes of space. Data acquisition relies heavily on mark sense scanning, supplemented with traditional key entry and barcode reading. The database supports and enforces the study protocol through its participant eligibility confirmation, randomization, drug dispensing and collection, visit and task planning, and outcomes processing functions. Security is provided both by password protection and by limiting access to specific data based on the identified role of the user. Local access to clinical site-specific data is supported through centrally defined reports and a flexible data extract system.

AEP Vol. 13, No. S9
October 2003: S5–S17

The CCC database provides the superstructure into which the clinical center data are consolidated routinely. Additional data are obtained from the central laboratories and specimen repository and are merged with, and checked against, the corresponding participant data. The central database serves as the source of all data reports and analyses.

Quality Assurance Program Overview

The WHI program involves a complex protocol, with an extensive set of required procedures. A quality assurance (QA) program was designed to allow the identification and correction of emerging problems. Quality assurance was considered an integral part of the study protocol, procedures, and database; hence, it covers all aspects of WHI. To balance the need to assure scientific quality of the study with available resources, priorities were established to guide clinical center and CCC quality assurance activities.

A task force comprised of WHI investigators and staff developed QA priorities under the premise that aspects critical to the main components of WHI would be of highest priority. As the centerpiece of WHI, the fundamental elements of the CT are considered the highest priority. The next highest priority is given to key elements of the OS and elements of the trial that are important for interpretive analyses. The remaining elements are given a lower priority. Table 5 provides the priorities of both clinical center and CCC quality assurance activities for both the CT and OS. The implementation of these priorities is manifested in the frequency and level of detailed quality assurance methods as follows: priority 1 items receive rigorous routine review and monitoring, both centrally and locally; priority 2 items receive review at a reduced level, often with only local monitoring or central review limited to data monitoring; and, priority 3 items are addressed on a time available basis. Since training and QA for some priority 3 items are identical to those of higher priority, there may be adequate carryover effects to assure adequate performance. Continued monitoring of these priority 3 areas is done to allow the detection of severe problems.

TABLE 5. WHI Quality Assurance Priorities

Priority 1	CT informed consent
	CT randomization
	CT interventions, adherence and retention
	CT safety
	CT primary outcomes
Priority 2	CT blinding
	CT eligibility
	OS primary outcomes
	OS/CT biological specimens
	OS/CT baseline predictive data
	CT follow-up predictive data
Priority 3	OS informed consent
	OS enrollment
	OS follow-up predictive data
	CT/OS subsidiary outcomes
	CT/OS ancillary study interference

Quality assurance activities are performed at the clinical centers as well as by the CCC. The program includes extensive documentation of procedures; training and certification of staff; routine quality assurance visits conducted by the CCC (all clinical centers received an initial and 1-year visit while subsequent visits are done approximately every other year, or more frequently as needed); and, database reports for pertinent committees and each clinical center describing the completeness, timeliness, and reliability of tasks at the clinical centers. For example, monthly intervention adherence rates, and major task completeness rates for each clinical center are used as up-to-date indicators of performance.

WHI established performance goals for various important tasks that are centrally monitored. These goals were determined on the basis of design assumptions and, where available, on previously published standards of quality and safety.

The performance of each clinical center is also reviewed on a regular basis under a comprehensive performance monitoring plan. This plan is used to identify clinic-specific performance issues in a timely fashion, to reinforce good performance, and to provide assistance or to institute corrective action if performance is inadequate. Much of this work is conducted under the auspices of a Performance Monitoring Committee (PMC), comprised of representatives of the CCC, clinical centers, and Project Office. The PMC follows up on persistent issues with specific clinical centers, and conducts site visits to facilitate the resolution of specific areas of concern.

SUMMARY AND DISCUSSION

The WHI CT and OS were implemented in close correspondence to design specifications (1). Departures from design assumptions concerning sample size, age distribution and projected average trial follow-up have limited effect on the adequacy of study power for the primary outcome for each of the clinical trial components, with the possible exception of the estrogen alone vs. placebo comparison where some power reduction for coronary heart disease arises from a smaller than targeted sample size. A substantial infrastructure for specimen storage, routine analyte determination, data management and computing, and for data and protocol quality control was implemented in close correspondence to design specifications.

Ongoing challenges in the CT and OS include retaining the active participation of study subjects over a lengthy follow-up period, ensuring the unbiased and timely ascertainment of outcome events in each trial component and

in the OS and, perhaps the most challenging, ensuring an adequate adherence to intervention goals for each clinical trial intervention. These areas are actively monitored as a part of WHI quality assurance efforts, and initiatives are undertaken as needed to ensure that the WHI provides reliable and informative answers to clinical trial hypotheses, and contributes additional valuable scientific knowledge concerning the major causes of morbidity and mortality among postmenopausal women in our society.

APPENDIX: DATA PROCESSING AND STATISTICAL METHODS, WHI CLINICAL COORDINATING CENTER STATISTICAL UNIT

DATA COLLECTION METHODS

All data collected for the WHI were obtained using standardized instruments. Initially, self-administered forms were formatted as traditional key entry forms and required duplicate data entry. With experience, all of these forms were reformatted to optical mark recognition (bubble) forms. Consequently, most of these variables were assessed with categorical responses. Data collection instruments used by clinic staff were typically formatted as key entry forms. The WHI data entry software incorporated standard, within form, quality assurance checks (range, valid response, and so forth). Problems at this step generated warnings or errors requiring action on the part of the clinical center staff. Additional quality assurance, including cross-form checks, were applied to the central database, and problems arising at this point resulted in either resolution based on Clinical Coordinating Center (CCC) assessment of the reliability of the individual data items and/or unresolvable data being eliminated. Because most forms underwent some revision, each item was mapped to the version on the most recent (and most prevalent) questionnaire, after review for the appropriateness of the possible mapping by CCC statisticians and epidemiologists.

DATA DEFINITIONS

Demographic and General Health Characteristics

Demographic factors were based on self-report of birth date, ethnicity, education, income, marital status and living situation. Categories for age at screening were created for these displays using 10-year strata based on birth date (50–59, 60–69, and 70–79 years old at initial contact). Consistent with the 1990 U.S. Census, women were asked to select one race/ethnicity from the following categories: Black/African-American (not of Hispanic origin); Hispanic/Latino; White (not of Hispanic origin); American Indian/Alaskan Native; Asian/Pacific Islander; and Other. A woman was considered to be living alone if she did not report living with her husband, children, siblings, other relatives, or friends. Birthplace (state and country) and years lived in the current state were collected only from Observational Study (OS) participants. Region of current residence was classified by state: Northeast (MA, NJ, NY, PA, RI), Southeast (AL, DC, FL, GA, NC, TN, TX), Midwest (IA, IL, MI, MN, OH, WI), and West (AZ, CA, HI, NV, OR, WA).

Occupation was based on a woman's current job, or if not currently employed, the job held the longest. The managerial/professional category listed as examples jobs that generally require a college degree or higher, including teacher, guidance counselor, registered nurse, doctor, lawyer, accountant, architect, computer analyst, personnel manager, and sales manager. Examples of technical/sales/administrative positions provided were office work and sales work. The category of service/laborer included employment such as food service, factory work, and protective service (police, fire).

Smoking status and alcohol intake were based on self-report questions about personal habits. Never smokers were women who smoked fewer than 100 cigarettes in their entire life. Past smokers were those who had ever smoked at least 100 cigarettes but did not currently smoke. Current smokers were those who had ever smoked at least 100 cigarettes and were currently smoking. Exposure to passive smoking was collected in the OS. OS participants were asked if they had ever lived with someone who smoked cigarettes inside their homes, both when they were less than 18 years old and when they were 18 years or older. If so, the number of years lived with a smoker was assessed. Alcohol intake was similarly defined. Nondrinkers were those who had less than 12 drinks of any kind of alcoholic beverage in their entire life. Past drinkers were those who had ever had at least 12 alcoholic beverages in their life but did not currently drink. Current drinkers were further classified by current alcohol intake, based on the sum of beer, wine, and liquor intake, adjusted for portion size, from the food frequency questionnaire.

Recreational physical activity was assessed by questions on the frequencies and duration of four speeds of walking, and three other types of recreational activity classified by intensity (strenuous, moderate, or light). These data were summarized into episodes per week of moderate or strenuous activity of 20 minutes or more duration, and expenditure of energy from recreational physical activity estimated by total METs per week. Episodes per week of moderate and strenuous activity included those with MET scores of at least 4.0 as classified by Ainsworth (5), including walking

AEP Vol. 13, No. S9
October 2003: S5–S17

"fairly fast (3.5 mph)" or "very fast (4.5 mph)", or participating in moderate or strenuous activities, such as jogging, aerobics, tennis, swimming, biking, use of an exercise machine, calisthenics, or popular or folk dancing. Those who reported no recreational physical activity were classified as no activity; those who reported some activity but none that met the criteria based on duration of at least 20 minutes, intensity at least moderate (MET score 4.0), and frequency at least twice per week, were placed in the category "limited activity"; and others were classified as participating in moderate or strenuous activity from 2 to <4 times per week, or 4+ times per week. Total energy expenditure (in METs per week) from recreational physical activity, including walking, mild, moderate and strenuous physical activity, was assessed and categorized into four groups based approximately on quartiles of the distribution of the overall Clinical Trial (CT) and OS participants. In addition to physical activity, participants were asked to report hours per day of sedentary activity including sitting, sleeping and lying down.

Supplement use was ascertained by a computer-driven inventory of all vitamin and mineral supplements taken by the woman. The data entry screens included definitions and common examples of the multiple-vitamin classes, prompts to enter information on all types of supplements, flexibility to enter any unit of measure on the label, and quality assurance range checks. During the interview, the interviewer examined the participants' supplement bottles and recorded information on the use of: three classes of multiple vitamins (one-a-day without minerals, one-a-day with minerals, and stress supplements); all single supplements (pills containing a single vitamin or mineral); and all other mixtures. Exact doses were required for all single supplements and other mixtures. For multivitamins, exact doses were required only for the subset of nutrients of special interest: vitamin C, beta-carotene, calcium, and selenium. For other vitamins and minerals in multiple-vitamin preparations, default doses were assumed based on leading brands and characteristics of supplements products in the U.S. Additional details of this assessment procedure and its validity have been published (6).

A computer-driven medication inventory system was developed to capture use of all other usual medications. This was conducted as an in-person interview at the first screening visit. Participants were asked to bring all prescription and over-the-counter preparations used regularly (at least twice a week) for the previous 2 weeks. The product or generic name was used to match the pharmacy database (Master Drug Data Base [MDDB]: Medi-Span, Indianapolis, IN) incorporated into the study data management system. Once the appropriate medication (and, wherever possible, strength of the formulation) was selected, duration of use was recorded. When appropriate, information from supplements and medication use was combined (e.g., use of antacids as a medication is included in total supplemental calcium intake).

Height, weight, hip, and waist circumference, and blood pressure were measured at the first clinic visit by certified clinic staff. Participants were asked to remove their shoes for anthropomorphic measures. Height (cm) was measured using a wall-mounted stadiometer. Weight (kg) was measured using a balance beam scale, after participants were asked to empty their pockets and remove any heavy clothing. Body mass index was calculated as weight (kg) / height (m). Waist and hip circumferences (in cm) were obtained using a standardized measuring tape. Participants were asked to remove all except for nonbinding undergarments and stand on both feet. After following the protocol for identifying the level of the natural waist and hips, and assuring that the tape was level, clinic staff recorded hip circumference. Waist circumference was similarly measured at the end of a participant's normal expiration. Blood pressures were measured twice after a 5-minute rest period using a conventional mercury sphygmomanometer and appropriately sized cuffs. Systolic blood pressure was defined as the pressure level at which the first of two or more regular Korotkoff sounds were heard. Diastolic blood pressure was defined as pressure level of the last of these rhythmic sounds.

Reproductive, Medical, and Family History

Self-reported reproductive history data included menstruation, pregnancy, lactation, and benign breast disease. Menstrual history information included ages at first and last menses, first birth, hysterectomy, oophorectomy, and tubal ligation, where applicable. Age at first birth was the woman's age at the end of her first pregnancy lasting at least 6 months. Abortion history was estimated by subtracting the number of live births, stillbirths, miscarriages and ectopic pregnancies from total pregnancies. History of benign breast disease was concluded if participants with no history of breast cancer reported a previous breast biopsy. If participants were still having menstrual bleeding or periods at time of screening (due to hormone use), participants were asked to enter their current age, in lieu of age at last menstrual bleeding.

Self-reported medical history included information on the participant's current health care provider, use of screening procedures (e.g., mammogram, Pap smear), hormone use and duration (e.g., estrogen only, estrogen + progesterone), health events, physician diagnoses of major diseases, and use of specified medications. For these presentations, hormone history reflected use of pills and patches only (creams and shots excluded); current or past use of less than three months or use of other preparations is not presented. History

of hypertension was defined by a physician's diagnosis regardless of treatment by oral medication. History of diabetes and history of high cholesterol were defined as a physician's diagnosis that required oral medication or insulin (diabetes only).

Depression was assessed using a self-administered, eight-item questionnaire. Participants were asked to rate the frequency of specific depressive symptoms over the previous week and to indicate the occurrence of diagnostically relevant periods of depression in the past. The weighting of the items and the cutoff for classification as depressed were based on Burnam (7).

Participants reported on specific health conditions and events associated with cardiovascular disease, circulatory problems, cancer, bone fractures, and other health outcomes associated with aging. For each, the report was based on a physician diagnosis. For cardiovascular disease, the conditions included history of myocardial infarction, coronary bypass surgery (CABG), angioplasty (PTCA), stroke, congestive heart failure, angina, carotid endarterectomy/angioplasty, deep vein thrombosis, pulmonary embolism, and peripheral arterial disease. Women who reported a history of cancer were asked to indicate what kind(s) from a list of 17 most common sites (e.g., breast, lung, colorectal, endometrial, melanoma, cervical) or other. History of colon polyp removal was collected. The risk factors ascertained for their association with bone fractures were osteoporosis, number of falls in the past 12 months, loss of consciousness, and personal history of fractures. Participants at three designated osteoporosis clinical centers (Tucson/Phoenix, AZ; Birmingham, AL; and Pittsburgh, PA) were given baseline dual x-ray absorptiometry to estimate bone density of the hip, spine, and total body, as well as to obtain lean and fat body mass. Women were classified as normal, osteopenic, or osteoporotic based on total hip bone density measures using World Health Organization criteria (8).

Family history of a limited number of conditions was obtained from the participant—without verification—for full-blooded, first-degree relatives. The conditions included heart attacks, stroke, diabetes, and cancer of the breast, colon, rectum, ovary, and prostate. Family members' histories for breast cancer included the aforementioned female relatives and both grandmothers. Only parental history was collected for fratures.

Dietary intake

Food and nutrient intake were assessed by a semiquantitative food frequency questionnaire (FFQ), based on instruments previously used in the Women's Health Trial Vanguard (9) and Full Scale Studies (10) and the Women's Health Trial Feasibility Study in Minority Populations (11). The FFQ is divided into three sections: adjustment questions, food line items, and summary questions. The 19 adjustment questions allow more refined analysis of fat intake (e.g., by asking about types of added fats) and fiber intake (e.g., by asking about usual types of breakfast cereals). The main section—food line items—consists of questions on the frequency and portion size of 122 foods consumed over the last 3 months. Food items were added to incorporate regional and ethnic foods in the United States. The four summary questions ask about the usual intake of fruits, vegetables, and fats added to foods or in cooking. These questions reduce the bias toward overreporting of total food consumption when there are long lists within food groups (e.g., 25 vegetables) (Nutrition Coordinating Center, Minneapolis, MN) (12, 13). Nutrient intake excludes nutrients from supplements.

The time reference for all questions was "in the last 3 months". Instructions on completing the FFQ were limited to directions and examples printed on the questionnaire itself and an additional page with portion size pictures on one side and instructions on the other side. For quality control purposes, all adjustment questions, all summary questions, 90 percent of the foods, and at least one half of every food group section (e.g., fruits, vegetables, breakfast foods) had to be completed.

The number of servings of fruits and vegetables per day was the sum of servings of fruits, fruit juices, potatoes, salads, and other vegetables, based on the summary questions and individual food items. The number of servings of grains per day was the sum of servings of rice, grains, plain noodles, beans (e.g., refried, baked), potato or pasta salads, bean soups (pea, lentil, black bean, chili with beans—with and without meat), pizza, pasta dishes (e.g., spaghetti, lasagna), many Mexican dishes (e.g., quesadillas, tacos, enchiladas), a wide range of breads (e.g., bagels, muffins, pitas, tortillas, white and dark breads), snacks (e.g., chips, popcorn), and cold or hot cereals.

Details of the measurement characteristics of the WHI FFQ have been published (14).

BLOOD SPECIMEN ANALYSES

Blood analytes were obtained from stored sera in the WHI repository at McKesson Bioservices (Rockville, MD). A fasting blood sample was obtained from each woman attending the initial screening visit. To improve the consistency of results, participants were asked to fast (nothing by mouth except water) for 12 hours before all blood collection; take all regular medications except for insulin or oral medication used to control diabetes; take no aspirin or nonsteroidal anti-inflammatory drugs for 48 hours before the visit, except those taken regularly; refrain from smoking for at least 1 hour before the blood draw; and perform no vigorous physical activity (such as jogging or bicycling) for at least 12

AEP Vol. 13, No. S9
October 2003: S5–S17

hours before the blood draw. Blood was drawn in a sitting position, and all samples were processed locally using a standardized protocol and with specific time limits. The resultant specimens—serum, plasma, buffy coat, and RBC—were labeled and stored at −70° C until shipment on dry ice to the central repository for long-term storage. A small fraction of clinical trial (CT) participants was selected at enrollment (8.6% cohort of postmenopausal hormone therapy (PHT) participants, 4.3% cohort of dietary modification (DM) participants, with oversampling of minorities) for prospective assessment of core analytes. A sample of 1% of observational study (OS) participants was randomly selected with stratification by race/ethnicity at baseline to be in the OS Measurement Precision Study (OS-MPS). These women had a second blood collection at 3 months and core analytes were measured in their baseline and 3 month bloods.

Blood specimens from women in the 6% CT blood sample and the OS-MPS were analyzed prospectively for lipids, lipoproteins, micronutrients, clotting factors, insulin and glucose levels. Participant serum and plasma samples were pulled from the repository based on length of storage and sent on dry ice to Medical Research Laboratories (Highland Heights, Kentucky) where these tests were conducted. Assay methods are described briefly below. Specimens were labeled with only vial identification numbers. Blind duplicates and quality control pooled samples were included in each batch. Results were provided to the CCC by vial number where the data were reviewed for internal quality control and merged to participant level information.

LABORATORY METHODS

Lipids, Lipoproteins and Apolipoproteins

All lipid, lipoprotein, and apolipoprotein fractions were analyzed using ethylene diamine tetra-acetic acid (EDTA)-treated plasma. Total cholesterol and triglycerides were analyzed by enzymatic methods on a Hitachi 747 analyzer (Boehringer Mannheim Diagnostics, Indianapolis, IN) as previously described (15). High-density lipoprotein cholesterol (HDL-C) was isolated using heparin manganese chloride (16). HDL3 was separated directly from whole plasma by precipitation of VLDL, LDL, and HDL2 with dextran sulfate (MW 50,000) and $MgCl_2$ (17). The supernate was measured enzymatically on the Hitachi 747. The HDL2 was calculated as the difference in cholesterol between the previously isolated HDL fraction and this HDL3 fraction. Lipoprotein (a) [Lp(a)] was quantitated using an isoform independent bi-site ELISA assay procedure based on the linkage of apo(a) to apoB (18). Standardization and ongoing quality control was established and maintained with Northwest Lipid Research Clinic. Throughout the study, the laboratory participated in and remained certified by the National Heart, Lung, and Blood Institute, Centers for Disease Control Part III program (19).

Micronutrients

Vitamin A, vitamin E, and the carotenoids were measured by high-performance liquid chromatography (20,21). After the addition of an internal standard, serum was extracted into hexane and injected onto a C_{18} reverse phase column. The analytes were measured at wavelengths of 292 nm and 452 nm.

Clotting Factors

All clotting factors were measured in citrated plasma. Factor VII activity was measured on a MLA ELECTRA 1400C (Medical Laboratory Instrumentation Inc., Mt. Vernon, NY) using a turbidometric detection system and using Factor VII–deficient plasma (George King Bio-Medical, Overland Park, KS) in preparation of the standard curve (22). Factor VII antigen was measured using a sandwich ELISA assay (Asserchrom VIIag, Diagnostica Stago, France) in which specific rabbit antihuman Factor VII antibodies were used (23). Fibrinogen is measured on a MLA ELECTRA 1400C (Medical Laboratory Automation Inc., Mt. Vernon, NY) using a clot-based turbidometric detection system (24).

Glucose was measured in serum using the hexokinase method on the Hitachi 747 (25, 26). Serum insulin was measured in a step-wise sandwich ELISA procedure on an ES 300 (Boehringer Mannheim Diagnostics, Indianapolis, IN). In the assay a monoclonal insulin antibody bound to the tube in turn binds insulin in proportion to its concentration in the sample. The bound insulin is then quantitated using a second monoclonal antibody labeled with peroxidase (POD) which then reacts with a chromogenic substrate to generate a photometrically monitored chromogen (27). An ongoing monthly quality assurance program was maintained with the Diabetes Diagnostic Laboratory at the University of Missouri.

STATISTICAL METHODS

As the intent of this publication is to describe the WHI participants, unadjusted descriptive statistics are presented throughout with the exception of summary blood results, where weighting by race/ethnicity of the corresponding cohort was used. Missing values occurred in most variables, either because of participant nonresponse or the data did not meet the defined quality assurance checks. Participants with missing data were included in all analyses except those involving variables for which data were not available or were considered unreliable.

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ELSEVIER

The Women's Health Initiative Postmenopausal Hormone Trials: Overview and Baseline Characteristics of Participants

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INTRODUCTION

The postmenopausal hormone therapy (PHT) component of the Women's Health Initiative (WHI) is composed of two randomized, placebo-controlled, double-blind trials in postmenopausal women aged 50 to 79 years at initial screening, testing the effects of estrogen alone (E-alone) and estrogen plus progestin (E + P) on coronary heart disease (CHD) as the primary outcome, hip and other fractures and colorectal cancer as secondary outcomes, and pulmonary embolism, breast and endometrial cancers as potential risks. The design and rationale of the PHT trials, including general eligibility and exclusion criteria and considerations regarding sample size and statistical power, have been described previously (1).

Postmenopausal hormones have been initiated in menopausal women for the treatment of vasomotor symptoms, mood disturbances, vaginal dryness, and prevention of rapid bone loss for several decades. Despite a paucity of data on effects of initiating hormone use in older women, postmenopausal hormones have also been promoted for the prevention of CHD, osteoporotic fractures, and other diseases that occur years after menopause (2). It is generally recommended (2) that women with a uterus be prescribed a combination of estrogen and progestin to prevent endometrial hyperplasia or cancer, whereas women with a hysterectomy receive unopposed estrogen. The purported benefits of estrogen are assumed to be similar for combined hormones, although relatively few studies have included long-term estrogen plus progestin users, particularly those taking continuous progestin. Reports of greater risk of breast cancer with cyclic estrogen/progestin combinations vs. unopposed estrogen (3, 4) highlight the need to determine the risks and benefits for both estrogen and combined hormones in appropriate clinical populations, including older women.

None of the clinical trials of postmenopausal hormones for cardiovascular endpoints completed previously, e.g., the PEPI study (5), HERS (6), ERA trial (7), or WEST (8), have provided information on the role of hormones in primary prevention of heart disease, nor was there clinical trial evidence that hormones prevent osteoporotic hip fractures (9) or increase breast cancer. A large randomized, controlled trial of postmenopausal hormones involving predominantly women without prior CHD or osteoporosis is needed to determine overall benefits and risks of long-term hormone use. WHI set out to randomize 27,500 ethnically diverse women into such a program for an 8.5-year period. Because women with a uterus were assigned to placebo or estrogen plus progestin, whereas women who had a hysterectomy were assigned to placebo or estrogen alone, the WHI hormone component is designed as two separate trials. Data are therefore presented for the total hormone component, as well as for the two distinct cohorts, i.e., those participating in the E + P trial and those participating in the E-alone trial.

METHODS

Eligibility Criteria and Screening

Details regarding eligibility criteria and the screening process, including hormone component-specific reasons for excluding participants, appear in Hays' article in this issue.

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A combination of age and months of amenorrhea determined eligibility for potential E + P participants who had not undergone hysterectomy. Women waited at least 3 months after a recent hysterectomy to be randomized. Women who were using hormones at initial contact completed a 3-month washout period before continuing screening for the PHT trials. A history of myocardial infarction or stroke within the prior 6 months was an exclusion criterion.

All potential PHT participants received information from trained staff on the objectives, risks, and procedures of the hormone trials. The materials described known potential side effects and risks of active study medications (i.e., breast and endometrial cancer, gallbladder disease, deep venous thrombosis, and pulmonary embolism) and those associated with *not* taking active hormones, including menopausal symptoms and osteoporosis. All participants provided written informed consent.

In addition to other assessments required for all clinical trial participants, PHT participants were required to have a pelvic exam, Pap smear and, for women with a uterus, endometrial aspiration (or transvaginal ultrasound, for women with cervical stenosis). Adherence to placebo during a 28-day (minimum) run-in period was determined by pill count. Women were excluded if they had less than 80% adherence to placebo run-in pills.

Data Collection and Definitions

Questionnaires, physical measurements, blood collection, quality assurance, and statistical procedures for the WHI clinical trial are described in Anderson's article in this issue and in the appendix to Anderson's article. The method for measuring bone mineral density (BMD) at three WHI clinical centers is described in Jackson's article in this issue.

Randomization

Eligible women who had a hysterectomy had to be willing to be randomly assigned to take either placebo pills or pills containing 0.625 mg of conjugated equine estrogens (CEE) each day. In the original design, women with a uterus had to be willing to be randomized to placebo pills, pills containing 0.625 mg CEE combined with 2.5 mg of medroxyprogesterone acetate (MPA) daily, or unopposed 0.625 mg CEE pills each day. In December 1994, when PEPI trial results indicated that unopposed estrogen was associated with an unexpectedly high incidence of complex endometrial hyperplasia (5), randomization of women with a uterus to unopposed estrogen was stopped, and 331 women who had been randomized to unopposed estrogen were unblinded and changed to E + P. Thereafter, women with a uterus were randomized to take either placebo pills or pills containing 0.625 mg CEE and 2.5 mg MPA each day.

RESULTS

From November 1993 through October 1998, 27,347 women were enrolled in the postmenopausal hormone therapy component (99.4% of goal); 16,608 (60.7%) had a uterus (E + P cohort), while 10,739 (39.3%) had a hysterectomy (E-alone cohort). PHT participants' age distribution was: 50 to 59 years, 32.3%; 60 to 69 years, 45.2%; and 70 to 79 years, 22.5% (mean age was 63.6 and 63.3 years in the E-alone and E + P cohorts, respectively). 19.5% of PHT participants identified themselves as women from specific racial/ethnic groups other than White (Table 1). A much higher proportion of Black, Hispanic, and American Indian women were younger than 60 years and a much lower proportion were 70 to 79 years old, compared with White women. Minority women, particularly Blacks, represented a greater proportion of women in the E-alone (hysterectomy) cohort than in the E + P cohort. The percentages of women with a hysterectomy were: Whites, 36.7%; Blacks, 59.0%; Hispanics, 42.4%; Asian/Pacific Islanders, 31.1%; and American Indians, 57.3%.

The majority of PHT women had schooling beyond high school, with over 30% having a college degree. Only 10.5% were current smokers. Alcohol intake was low, with only 4.8% of E + P women and 3.2% of E-alone women consuming an average of two or more alcoholic drinks per day. Overall, women in the E + P cohort were more highly educated, had higher family incomes, were more physically active, and were more likely to take calcium supplements than women in the E-alone cohort. Dietary calcium intake (not shown) was 664 ± 352 mg/day (mean ± standard deviation) for E + P participants and 613 ± 337 mg/day for E-alone women, with little variation across age groups.

Only 26.7% of hormone component participants were normal or underweight, while 38.2% were obese (Table 2). A higher percentage of women in the E-alone cohort (44.6%) were obese, compared with the E + P cohort (34.1%), and a much lower proportion of E-alone women were normal weight. Mean waist circumference was 91.6 ± 13.8 cm for women in the E-alone cohort and 88.0 ± 13.8 cm for those in the E + P cohort. One-third of PHT participants had ever been told by a doctor that they had hypertension, and the proportion with a systolic blood pressure above 140 mm Hg increased substantially across the age groups in both the E-alone and E + P cohorts. A quarter of all PHT women were being treated for high blood pressure and nearly 14% had high cholesterol requiring pills. A higher percentage of women in the E-alone cohort had high blood pressure and reported being treated for hypertension, diabetes, and high cholesterol than those in the E + P cohort. Only a small percentage of PHT participants reported a prior heart attack, coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty

TABLE 1. Baseline demographic and general health characteristics of WHI Postmenopausal Hormone Therapy participants by hysterectomy[a] status and age at screening

	E + P						E-alone						Total						
	50–59 (N = 5522)		60–69 (N = 7510)		70–79 (N = 3576)		50–59 (N = 3310)		60–69 (N = 4852)		70–79 (N = 2577)		E + P (N = 16,608)			E-alone (N = 10,739)			Total (N = 27,347)		
Characteristic	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD
Race/Ethnicity																					
American Indian	0.5		0.3		0.2		0.8		0.7		0.5		56	0.3		75	0.7		131	0.5	
Asian/Pacific Islander	2.4		2.0		2.2		1.6		1.5		1.5		363	2.2		164	1.5		527	1.9	
Black	9.7		5.9		4.0		20.1		14.4		9.8		1124	6.8		1617	15.1		2741	10.0	
Hispanic	8.9		4.3		2.2		10.2		5.4		2.1		888	5.3		655	6.1		1543	5.6	
White	77.0		86.2		90.0		65.8		76.7		84.6		13,945	84.0		8082	75.3		22,027	80.5	
Unknown	1.5		1.3		1.4		1.5		1.2		1.5		232	1.4		146	1.4		378	1.4	
Education																					
0–8 years	2.8		2.3		1.5		3.3		3.2		2.7		379	2.3		329	3.1		708	2.6	
Some high school	3.9		4.3		5.5		5.5		7.2		7.8		735	4.5		724	6.8		1459	5.4	
High school diploma/GED	16.5		22.1		18.8		20.5		24.6		22.3		3222	19.5		2421	22.8		5643	20.8	
School after high school	39.1		38.2		40.0		45.6		42.7		42.2		6415	38.9		4621	43.4		11,036	40.7	
College degree or higher	37.7		33.1		34.2		25.2		22.4		25.1		5753	34.9		2543	23.9		8296	30.6	
Family income																					
<$10,000	6.5		4.8		5.3		8.5		8.8		8.0		857	5.5		864	8.5		1721	6.7	
$10,000–$19,999	10.2		15.5		21.3		14.4		19.7		26.5		2348	15.0		1989	19.7		4337	16.8	
$20,000–$34,999	21.8		29.3		32.5		24.7		31.0		33.6		4316	27.5		2999	29.7		7315	28.3	
$35,000–$49,999	20.6		22.4		19.6		19.7		20.7		16.0		3329	21.2		1947	19.3		5276	20.4	
$50,000–$74,999	21.5		16.6		14.0		19.1		13.0		10.6		2773	17.7		1447	14.3		4220	16.4	
$75,000 +	19.4		11.4		7.4		13.5		6.9		5.3		2075	13.2		866	8.6		2941	11.4	
Marital status																					
Never married	5.2		3.6		3.6		3.9		2.8		2.9		686	4.1		337	3.2		1023	3.8	
Divorced/Separated	23.6		15.1		9.7		26.9		18.4		10.5		2774	16.8		2038	19.1		4812	17.7	
Widowed	7.5		18.5		37.5		8.4		21.1		39.7		3137	19.0		2316	21.7		5453	20.0	
Presently married/Living as married	63.6		62.8		49.1		60.7		57.7		46.9		9945	60.1		5984	56.1		15,929	58.5	
Smoking																					
Never smoked	46.8		49.5		55.3		47.4		50.1		58.0		8177	49.8		5428	51.1		13,605	50.3	
Past smoker	38.1		41.1		39.5		37.8		39.4		37.2		6519	39.7		4075	38.4		10,594	39.2	
Current smoker	15.2		9.5		5.2		14.8		10.5		4.9		1718	10.5		1113	10.5		2831	10.5	
Alcohol intake																					
Never drinker	10.1		11.7		13.7		12.6		14.0		14.6		1910	11.6		1455	13.7		3365	12.4	
Past drinker	17.2		16.3		18.3		23.3		24.5		23.8		2807	17.0		2547	23.9		5354	19.7	
Current drinker	72.7		72.0		68.0		64.1		61.6		61.6		11,761	71.4		6633	62.4		18,394	67.8	
Physical activity																					
No activity	19.8		18.1		16.3		25.4		21.7		17.1		2783	18.2		2124	21.7		4907	19.6	
Some activity	42.6		43.1		43.0		44.1		45.7		48.3		6556	42.9		4485	45.8		11,041	44.1	
2–< 4 episodes/wk of moderate + activity	14.8		15.6		17.7		14.1		14.7		15.0		2415	15.8		1428	14.6		3843	15.3	
4 + episodes/wk of moderate + activity	22.8		23.1		23.1		16.4		17.9		19.6		3512	23.0		1747	17.9		5259	21.0	
Dietary energy (kcal)[b]		1606 ± 645		1547 ± 576		1474 ± 544		1582 ± 668		1514 ± 607		1443 ± 551	16,049		1550 ± 593	10,250		1517 ± 614	26,299		1537 ± 602
Calcium as single supplement (including antacids)																					
No	81.1		76.4		71.6		85.7		81.0		78.7		12,776	76.9		8737	81.4		21,513	78.7	
Yes	18.9		23.6		28.4		14.3		19.0		23.6		3832	23.1		2002	18.6		5834	21.3	

[a]Women with a uterus comprised the E + P cohort, and those with a hysterectomy at randomization comprised the E-alone cohort.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

TABLE 2. Baseline medical history status of WHI Postmenopausal Hormone Therapy participants by hysterectomy[a] status and age at screening

	E + P						E-alone						Total								
	50–59 (N = 5522)		60–69 (N = 7510)		70–79 (N = 3576)		50–59 (N = 3310)		60–69 (N = 4852)		70–79 (N = 2577)		E + P (N = 16,608)			E-alone (N = 10,739)			Total (N = 27,347)		
Medical History	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD
Body mass index (BMI), kg/m^2		28.9 ± 6.3		28.6 ± 5.8		27.5 ± 5.2		31.2 ± 6.7		30.2 ± 6.0		28.6 ± 5.4	16,520		28.5 ± 5.4	10,672		30.1 ± 6.2	27,192		29.1 ± 6.0
Underweight (<18.5)	0.5		0.6		1.1		0.2		0.4		0.6		118	0.7		39	0.4		157	0.6	
Normal (18.5–24.9)	29.5		28.0		34.6		16.8		19.5		26.3		4940	29.9		2167	20.3		7107	26.1	
Overweight (25.0–29.9)	33.3		36.1		36.6		32.0		34.4		38.9		5826	35.3		3707	34.7		9533	35.1	
Obesity I (30.0–34.9)	20.8		22.0		19.1		26.2		26.1		23.3		3467	21.0		2716	25.4		6183	22.7	
Obesity II (35.0–39.9)	10.1		9.0		6.8		15.1		13.1		7.9		1475	8.9		1332	12.5		2807	10.3	
Obesity III (≥40)	5.7		4.2		1.8		9.7		6.6		2.9		694	4.2		711	6.7		1405	5.2	
Systolic blood pressure (mm Hg)																					
≤120	51.2		34.7		23.4		43.0		29.2		21.5		6270	37.8		3394	31.6		9664	35.3	
>120–140	37.0		43.7		43.4		41.5		44.9		42.3		6873	41.4		4641	43.2		11,514	42.1	
>140	11.9		21.6		33.2		15.6		25.9		36.2		3465	20.9		2704	25.2		6169	22.6	
Diastolic blood pressure (mm Hg)																					
<90	91.7		92.4		94.5		88.9		91.3		94.1		15,385	92.6		9799	91.3		25,184	92.1	
≥90	8.3		7.6		5.5		11.1		8.7		5.9		1223	7.4		938	8.7		2161	7.9	
History of hypertension																					
Never hypertensive	78.5		68.3		68.3		67.2		58.2		52.9		10,609	70.0		5762	59.7		16,371	66.0	
Untreated hypertensive	7.6		8.6		8.8		11.4		10.0		9.4		1266	8.4		993	10.3		2259	9.1	
Treated hypertensive	13.9		23.1		29.9		21.3		31.8		37.7		3271	21.6		2903	30.1		6174	24.9	
Treated diabetes (pills or shots)																					
No	96.1		95.4		95.0		93.3		91.8		92.2		15,864	95.6		9907	92.3		25,771	94.3	
Yes	3.9		4.6		5.0		6.7		8.2		7.8		734	4.4		821	7.7		1555	5.7	
Treated hypercholesterolemia (pills)																					
No	93.6		85.0		82.7		90.7		83.2		80.6		13,107	87.3		8147	84.8		21,254	86.3	
Yes	6.4		15.0		17.3		9.3		16.8		19.4		1906	12.7		1460	15.2		3366	13.7	
History of MI																					
No	99.4		98.1		96.6		98.7		96.8		94.7		16,312	98.2		10,402	96.9		26,714	97.7	
Yes	0.6		1.9		3.4		1.3		3.2		5.3		296	1.8		337	3.1		633	2.3	
History of CABG/PTCA																					
No	99.7		98.7		97.1		99.0		97.6		96.6		16,191	98.7		10,345	97.8		26,536	98.3	
Yes	0.3		1.3		2.9		1.0		2.4		3.4		215	1.3		234	2.2		449	1.7	
History of stroke																					
No	99.6		99.3		98.3		99.2		98.3		97.4		16,470	99.2		10,571	98.4		27,041	98.9	
Yes	0.4		0.7		1.7		0.8		1.6		2.6		138	0.8		168	1.6		306	1.1	
Family history of breast cancer																					
No	85.3		84.5		82.5		82.5		82.6		82.3		13,256	84.3		8309	82.5		21,565	83.6	
Yes	14.7		15.5		17.5		17.5		17.4		17.7		2461	15.7		1763	17.5		4224	16.4	
History of fracture at age 55+[b]																					
No	95.8		84.8		73.8		95.2		84.8		76.1		11,317	84.6		7168	84.5		18,485	84.6	
Yes	4.2		15.2		26.2		4.8		15.2		23.9		2057	15.4		1319	15.5		3376	15.4	

MI, myocardial infarction.
[a]Women with a uterus comprised the E + P cohort, and those with a hysterectomy at randomization comprised the E-alone cohort.
[b]Applies only to participants age 55 and older at baseline.

TABLE 3. Baseline gynecologic history status of WHI Postmenopausal Hormone Therapy participants by hysterectomy[a] status and age at screening

	E + P			E-alone			Total					
	50–59 (N = 5522)	60–69 (N = 7510)	70–79 (N = 3576)	50–59 (N = 3310)	60–69 (N = 4852)	70–79 (N = 2577)	E + P (N = 16,608)		E-alone (N = 10,739)		Total (N = 27,347)	
Gynecologic History	%	%	%	%	%	%	N	%	N	%	N	%
Number of live births												
Never pregnant	8.5	7.1	8.0	6.7	6.2	7.5	1288	7.8	713	6.7	2001	7.4
None	3.4	2.0	2.4	2.9	2.1	2.7	422	2.6	262	2.5	684	2.5
1	10.5	7.2	7.8	9.7	6.9	8.3	1389	8.4	862	8.1	2251	8.3
2–4	66.0	62.0	63.0	65.0	59.9	61.2	10,503	63.5	6589	61.8	17,092	62.9
5+	11.6	21.7	18.8	15.7	24.9	20.3	2928	17.7	2237	21.0	5165	19.0
Age at first birth, (y)[b]												
Never had term pregnancy	4.0	2.2	2.8	3.2	2.2	2.9	400	2.9	237	2.7	637	2.8
<20	20.6	16.7	8.9	36.4	27.5	14.7	2236	16.4	2417	27.3	4653	20.7
20–29	66.8	72.8	72.9	56.7	65.6	73.8	9670	70.8	5737	64.8	15,407	68.4
30+	8.6	8.2	15.4	3.6	4.7	8.7	1344	9.8	469	5.3	1813	8.1
Total oral contraceptive duration, (y)												
Non-user	36.2	60.4	82.0	36.8	65.1	87.6	9466	57.0	6634	61.8	16,100	58.9
<5	33.9	20.8	9.2	36.4	20.7	7.9	3765	22.7	2409	22.4	6174	22.6
5–<10	16.1	8.2	3.6	15.1	7.2	2.5	1634	9.8	914	8.5	2548	9.3
10+	13.8	10.5	5.3	11.7	7.0	2.1	1743	10.5	782	7.3	2525	9.2
Age at hysterectomy, (y)												
<40				55.5	36.6	25.5			4249	39.8	4249	39.8
40–49				38.3	46.2	41.8			4556	42.7	4556	42.7
50+				6.2	17.2	32.7			1872	17.5	1872	17.5
Bilateral oophorectomy												
No	99.8	99.6	99.6	64.0	57.5	56.2	16,474	99.7	5890	59.3	22,364	84.5
Yes	0.2	0.4	0.4	36.0	42.5	43.8	53	0.3	4049	40.7	4102	15.5
History of PHT use[c]												
Never	70.5	75.1	74.5	49.4	50.7	52.8	12,192	73.4	5447	50.8	17,639	64.6
Past, <5 years ago	11.8	6.4	3.1	13.5	8.5	4.5	1243	7.5	975	9.1	2218	8.1
Past, 5–<10 years ago	4.0	4.9	1.9	6.6	4.8	3.3	659	4.0	535	5.0	1194	4.4
Past, 10+ years ago	1.4	7.1	17.5	9.2	21.7	31.3	1233	7.4	2159	20.1	3392	12.4
Current	12.3	6.4	3.1	21.3	14.3	8.1	1273	7.7	1608	15.0	2881	10.5
Total PHT duration, years												
< 5	76.9	68.4	64.0	57.8	52.0	52.3	3118	70.6	2853	53.9	5971	61.5
5–<10	18.3	17.7	16.7	22.1	18.1	15.6	783	17.7	995	18.8	1778	18.3
10+	4.8	13.9	19.3	20.2	29.8	32.1	514	11.6	1444	27.3	1958	20.2
History of E-alone use[3]												
Never	93.7	89.2	80.7	52.2	52.7	53.8	14,756	88.9	5664	52.8	20,420	74.7
Past/Current	6.3	10.8	19.3	47.8	47.3	46.2	1845	11.1	5061	47.2	6906	25.3
History of E + P use[3]												
Never	74.5	83.0	91.7	94.0	95.5	97.7	13,620	82.0	10,261	95.6	23,881	87.3
Past/Current	25.5	17.0	8.3	6.0	4.5	2.3	2984	18.0	477	4.4	3461	12.7

PHT, postmenopausal hormone therapy; E-alone, estrogen alone; E + P, estrogen + progestin.
[a]Women with a uterus comprised the E + P cohort, and those with a hysterectomy at randomization comprised the E-alone cohort.
[b]Applies only to participants who have ever been pregnant.
[c]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.

TABLE 4. Baseline characteristics of WHI Postmenopausal Hormone Therapy and Bone Mineral Density participants by hysterectomy[a] status and age at screening

	E + P				E-alone				Total					
	50–64 (N = 553)		65–79 (N = 472)		50–64 (N = 518)		65–79 (N = 419)		E + P (N = 1025)		E-alone (N = 937)		Total (N = 1962)	
Characteristic	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD
Total hip BMD (WHO criteria)														
Normal	60.8		39.7		66.4		38.9		51.0		54.0		52.4	
Osteopenic	37.1		50.9		30.6		51.0		43.5		39.8		41.7	
Osteoporotic	2.1		9.4		3.0		10.1		5.5		6.2		5.8	
Hip scan (g/cm^2)		0.87 ± 0.13		0.79 ± 0.12		0.90 ± 0.13		0.81 ± 0.13		0.84 ± 0.13		0.86 ± 0.14		0.85 ± 0.14
Spine scan (g/cm^2)		0.97 ± 0.15		0.92 ± 0.17		0.98 ± 0.16		0.95 ± 0.16		0.95 ± 0.16		0.97 ± 0.16		0.96 ± 0.16
Whole body scan (g/cm^2)		1.02 ± 0.10		0.96 ± 0.09		1.03 ± 0.10		0.98 ± 0.10		0.99 ± 0.10		1.01 ± 0.11		1.00 ± 0.10
Lean body mass +BMC (kg)		41.0 ± 5.9		38.8 ± 4.8		41.8 ± 5.9		39.5 ± 5.6		40.0 ± 5.5		40.7 ± 5.9		40.3 ± 5.7
Fat body mass (kg)		33.6 ± 11.8		31.2 ± 10.1		37.2 ± 12.0		34.1 ± 10.5		32.5 ± 11.1		35.8 ± 11.4		34.1 ± 11.4
	N		N		N		N		N		N		N	
	553		472		518		419		1025		937		1962	

BMD, bone mineral density; WHO, World Health Organization; BMC, bone mineral content.
[a]Women with a uterus comprised the E + P cohort, and those with a hysterectomy at randomization comprised the E-alone cohort.

(PTCA), or stroke, with a higher percentage of E-alone participants reporting these than E + P subjects. About 16% of PHT participants reported having a female relative who had breast cancer, with a slightly higher proportion of E-alone women reporting this than E + P women.

Over 80% of PHT women reported two or more live births and nearly 20% had five or more (Table 3). Women in the E-alone cohort were more likely to have had first births before age 20 and less likely to have them after age 30 than women in the E + P cohort. Only a small percentage of older women in either the E-alone or E + P cohorts reported ever using oral contraceptives (OC), particularly for more than 5 years. Mean OC duration was 5.6 ± 5.4 years for all E + P women and 4.8 ± 4.9 years for all E-alone women. A higher proportion of women aged 50 to 59 years were taking postmenopausal hormones at the initial screening visit compared with older women, thereby requiring a 3-month wash-out, particularly for women who were eventually enrolled in the E-alone trial. The proportion of women in the E + P cohort who had never used hormones was much higher than in the E-alone group. In both cohorts, a much higher proportion of women aged 70 to 79 years had stopped using hormones 10 or more years ago and a higher percentage had used hormones for 10 or more years in duration, compared with younger women. Lifetime duration of hormone use was 4.1 ± 4.8 years for women in the E + P cohort and 7.0 ± 7.5 years for women in the E-alone cohort. Older women reported lower rates of combined estrogen/progestin use compared with the younger women in both cohorts, particularly in the E + P cohort. A higher fraction of older women reported prior use of unopposed estrogen in the E + P cohort compared with the younger E + P participants.

In each ethnic group, women in the E-alone cohort were more likely to report no physical activity (except in American Indians), to be obese and have high blood pressure, and to report being treated for hypertension, diabetes, and high cholesterol, compared with women in the E + P cohort. In Blacks, Hispanics, and Whites, women in the E-alone cohort reported having a history of prior myocardial infarction, CABG/PTCA, and/or stroke at a higher frequency than women in the E + P cohort (see appendix to Hays' article). Also, in each ethnic group, a higher percentage of the women in the E-alone cohort had five or more live births, first births before age 20, and had used postmenopausal hormones ever and for 10 or more years.

BMD measurements of the subsample of PHT participants who had DEXA tests (i.e., those randomized at the three bone density centers) are presented in Table 4 for E + P, E-alone, and combined. While most features of this subsample are similar to the entire PHT cohort, some modest differences are noted. The mean age for the total BMD subsample was 63.7 years and 47.4% of women had a hysterectomy. Compared with the total PHT cohort, the subsample included smaller proportions of women who had ever

smoked or reported no physical activity, but also smaller proportions of women who reported either 2 to 3 or 4 or more 20-minute exercise bouts per week. The subsample also included a greater proportion of women who had never used postmenopausal hormones, with those who had used them having done so for a shorter duration. As in the total sample, within the BMD subsample, women in the E-alone cohort were less physically active, had a higher body mass index, and were more likely to have used postmenopausal hormones ever and to have used them 10 or more years and for a longer duration than women in the E + P trial. Despite these differences, and small differences in dietary calcium and use of calcium supplements, bone density did not differ markedly between women in the E-alone and E + P BMD subsamples at the hip, spine, or whole body. A smaller proportion of women in the E + P cohort BMD subsample met the WHO criteria (10) for normal BMD at the hip (<1 SD below the mean of young normal women), yet a smaller percentage were osteoporotic (>2.5 SD below the mean), compared with the women in the E-alone cohort BMD subsample.

Differences in levels of selected blood analytes in the 8.6% subsample between women in the E + P cohort (N = 1319) and E-alone cohort (N = 992) included higher levels of fasting triglycerides, slightly lower HDL and HDL-2 cholesterol levels, and slightly higher insulin levels in the women in the E-alone subsample compared with the E + P subsample (Table 5).

DISCUSSION

The initial WHI design assumed 55% of women (15,125) would be assigned to E + P or placebo and 45% (12,375) would be assigned to E-alone or placebo for an average of 9 years. Nearly 1500 more women were recruited into the E + P arm than originally planned, but over 1600 fewer were randomized into the E-alone arm. Average follow-up was planned for 8.5 years. Age goals were nearly achieved; primarily due to closure of age cells for White women aged 50 to 59 years before recruitment ended. The ethnic distribution among PHT participants is similar to the percentage in the US census for women aged 50 to 79 years: Whites, 86.3%; Blacks, 9.6%; Hispanic, 5.1%; Asian-Pacific Islander, 2.0%; American Indian 0.5%; and other 1.6% (11). This is considerably more diverse than most previous hormone trial cohorts (5–7). The percentage of women in the PHT component with a hysterectomy is 39.3%. Hysterectomy, one of the most common surgeries performed in the US (12), has been reported in approximately 40% of US women over 40 years (13). Hysterectomy surveillance data indicate that annual rates of hysterectomy in the US do not differ by race, although the reasons for this surgery and the age at which it is performed do differ across ethnic groups, with Blacks and Hispanics having the surgery at younger ages than Whites (13, 14, 15). Differences in the proportion of women with a uterus across the WHI ethnic groups may be a consequence of the recruitment process, which restricted entry of White women by age but not of minority women, resulting in a higher proportion of younger minority women.

The family household income and the percentage of PHT women with a college degree or higher exceeds that of women of this age in the general population (11). The smoking rate is lower (11), as is the percentage of PHT women reporting no participation in leisure-time physical activity (24.8%) per week, which was thirty to fifty percent for women of this age in NHANES III (16). On the other hand, the percentage that was achieving the level of activity recommended by the US Surgeon General (accumulation of

TABLE 5. Baseline blood analytes from WHI Postmenopausal Hormone Therapy participants by hysterectomy[a] status

	Hysterectomy status					
	E + P (N = 1319)		E-alone (N = 992)		Total (N = 2311)	
Blood analyte[b,c]	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
Total cholesterol (mg/dl)	1318	222 ± 37.1	991	226.5 ± 41.3	2309	223.7 ± 38.2
LDL-C (mg/dl)	1297	134.7 ± 32.9	970	137.3 ± 37.8	2267	135.7 ± 34.9
HDL-C (mg/dl)	1313	55.3 ± 13.6	987	54.2 ± 13.8	2300	54.9 ± 13.8
HDL-2 (mg/dl)	1276	16.4 ± 7.0	963	15.9 ± 6.7	2239	16.2 ± 7.0
HDL-3 (mg/dl)	1276	38.2 ± 7.9	964	37.8 ± 8.3	2240	38.1 ± 8.1
Triglyceride (mg/dl)	1318	130.9 ± 59.4	991	144.1 ± 67.3	2309	135.7 ± 63.6
Lp (a) (mg/dl)	1299	16.0 ± 17.2	974	16.1 ± 17.2	2273	16.0 ± 17.5
Fibrinogen (mg/dl)	1269	301.5 ± 56.2	960	305.6 ± 62	2229	303.1 ± 58.1
Glucose (mg/dl)	1315	98.4 ± 19	989	101.9 ± 23.9	2304	99.7 ± 21.1
Insulin (μlU/ml)	1280	10.0 ± 4.9	971	11.0 ± 5.5	2251	10.4 ± 5.3

[a]Women with a uterus comprised the E + P cohort, and those with a hysterectomy at randomization comprised the E-alone cohort.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.
[c]Means and standard deviations are weighted by the overall CT and OS ethnic distribution.

30 minutes of exercise on most, preferably all, days of the week) was also lower than the NHANES III sample (16). The percentage of obese women was considerably higher in the PHT cohort than the national averages of 28.9%, 24.8%, and 20.0% for US women aged 50 to 59, 60 to 69, and 70 to 79 years, respectively (17). The mean daily intake of dietary calcium was above the average intake of 571 mg/day for women aged 50 to 70 years in the US (18); however, this amount is less than the recommended intake of 1200 mg/day of calcium in this age group (19).

PHT women appeared to be at fairly low risk for CHD, when compared with risk profiles identified by systematic screening (20). Hypertension was reported by fewer PHT women than women in the general population, ranging from 38% to 68% in 50- to 79-year-old White women, and from 47% to 78% in Black women of this age (21). Diabetes was also reported less often by PHT women than the 10.4% reported for 65- to 74-year-old women in the general population (22), as was high cholesterol requiring pills (23). Prevalence of self-reported stroke and prior myocardial infarction were also lower than what was reported by women aged 55 to 79 years in NHANES III (24).

The two cohorts within the PHT component differ in most characteristics described here. Since hysterectomy status may influence a woman's willingness to be randomized to placebo or active hormones, differences between the E + P and E-alone cohorts cannot be attributed to having a hysterectomy as these differences may merely represent some selection biases. Because population studies and clinical trials do not generally provide demographic, lifestyle, or medical characteristics by hysterectomy status, it is difficult to determine whether differences seen between women with and without a uterus in WHI reflect those of the general population. However, the characteristics of each cohort may influence the outcome of each trial, so it is important to recognize the differences between the cohorts of women participating in the E-alone and the E + P trials. In particular, it should be clear that these are two separate trials, involving two distinct study populations that are receiving different treatments. In general, women in the E-alone trial were at higher risk for CHD than the E + P cohort at baseline. They were more obese, less active, and had a slightly higher incidence of pre-existing cardiovascular disease. A high percentage, though not the majority, of WHI women in the E-alone cohort reported a bilateral oophorectomy, which is often performed in the context of a hysterectomy as a means of preventing ovarian cancer (25). Bilateral oophorectomy, but not hysterectomy, has been associated with greater risk for CHD in several studies (26, 27).

It is anticipated that comparisons between the E + P and E-alone cohorts will be done in secondary analyses. The fact that women are randomized to active or placebo hormones in each cohort will enable us to control for differences between their respective placebo groups, as well as the measured confounders noted in this paper. While this cannot replace a direct randomized comparison, it will provide much stronger evidence regarding the relative merits of these two regimens than any other type of observational study.

The WHI hormone trials will eventually be considered in relationship to study populations of other randomized trials of hormone use, both completed (5, 6, 7, 28, 29) and underway. Blood analytes in the WHI subsample generally reflect higher coronary risk than in the younger PEPI cohort (5) and lower risk than in the HERS secondary prevention trial (6). For example, mean fasting plasma fibrinogen, triglycerides, and glucose were higher, and HDL-cholesterol was lower, in the WHI subsample than in PEPI, whereas HDL-cholesterol was higher and triglycerides were lower in the WHI subsample than in HERS.

The WHI PHT component is distinguished by the size and diversity of its cohort and as a primary prevention trial with multiple clinical outcomes. Beyond differences between age and ethnic groups, the current report emphasizes the differences between WHI women with a uterus assigned to E + P or placebo and women with a hysterectomy assigned to E-alone or placebo, which will have a bearing on the interpretation of the final results.

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ELSEVIER

The Women's Health Initiative Dietary Modification Trial: Overview and Baseline Characteristics of Participants

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INTRODUCTION

The Dietary Modification (DM) component of the Women's Health Initiative (WHI) is a randomized controlled evaluation of a low-fat diet that is high in fruits, vegetables, and grains. This low-fat dietary pattern is hypothesized to reduce the risk of breast and colorectal cancer and secondarily, coronary heart disease, in postmenopausal women. To test these hypotheses, 48,836 postmenopausal women were randomly assigned to either the low-fat eating pattern (40%) or self-selected dietary behavior (60%). The nutrition goals for women in the intervention arm are to reduce energy from fat to 20% and energy from saturated fat to 7%, and to increase fruit and vegetable intake to at least five servings per day and grains to at least six servings per day. Participants will be followed for an average of 8.5 years.

The DM was motivated by animal studies (1, 2), international ecologic studies of diet and disease (3, 4), migrant studies (5–7), and epidemiologic studies (8) indicating that the diet, particularly lower levels of fat intake, has the potential to reduce risk of breast cancer, colon cancer, and heart disease. Within-country analytic epidemiologic studies of fat and breast and colorectal cancers have yielded inconsistent or null results (9–11). However there are substantial obstacles to finding clear and interpretable relationships in these studies (12):

- Current or recent fat intakes may differ from intakes during the years pertinent to the development of chronic diseases, likely attenuating associations.
- Fat intakes in Western populations may not be highly variable, in spite of the variety of foods available.
- It is difficult to estimate the relationship between fat intake and disease because diet is a complex mixture of foods, nutrients, and other bioactive compounds.
- Dietary patterns often relate to other disease risk factors, offering the potential for confounding (or over-control) in these studies.
- Considerable random, systematic, and person-specific errors exist in all available dietary assessment methods and the key measurement properties of these instruments are not well understood.

The purpose of this report is to describe the baseline characteristics of participants in the DM trial, with emphasis on sociodemographics, health behavior, medical history, dietary intake, and other factors that could relate to the clinical outcomes.

METHODS

Screening and Eligibility for the Dietary Modification Trial

The WHI included postmenopausal women aged 50 to 79 years. Women with previous or existing breast cancer or invasive cancer of any type within the past 10 years were excluded. General WHI trial eligibility criteria are provided in Hays' article in this issue. The DM component also

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excluded women who were: 1) on a low-fat diet (<32% energy from fat); 2) had dietary needs incompatible with the intervention program (e.g. celiac sprue); 3) ate 10 or more meals per week outside the home; 4) could not complete a 4-day food record; 5) had type I diabetes mellitus, been diagnosed with colon cancer, or had any gastrointestinal conditions that contraindicated a high-fiber diet; or 6) had a bilateral prophylactic mastectomy.

During the baseline clinic visits, approximately half of the women screened were excluded from the DM because they consumed a diet with less than 32% energy from fat, as estimated by the food frequency questionnaire (FFQ). The purpose of this screening was to enroll a group having a relatively high fat intake and thereby increase the difference in average percent energy from fat between women randomized to the dietary intervention vs. control groups, which increases study power for each clinical outcome. Because of this screening, the distribution of percent energy from fat from the FFQ at baseline is truncated (Figure 1A). This truncation imposes an upward bias on the usual estimates of mean intake of energy and fat and all nutrients correlated with energy or fat. To avoid this problem of regression to the mean, we present FFQ data from control participants at Year 1 of the trial. As shown in Figure 1B, in this group percent energy from fat is approximately normally distributed. In addition, data from a random sample of food records analyzed from baseline and Year 1 indicate no substantial secular changes in dietary patterns in control participants over the first year of the trial. For example, energy from fat from food records in this group was 33.0% at baseline and 33.1% at Year 1. Therefore, the Year 1 control group data should provide a reasonably unbiased representation of the dietary intake of all dietary modification participants at baseline.

The WHI Dietary Modification Intervention Program

Each participant received an individualized fat gram goal that was approximately 20% of her estimated daily energy intake during the intervention. The philosophy of the intervention is that of a self-directed, self-controlled eating plan that views dietary changes as a series of activities that ultimately become part of everyday life. Participants self-monitor fat, fruit/vegetable, and grain intake, which helps them make appropriate food choices while receiving feedback on their performance in relation to the WHI nutrition goals. The DM intervention is delivered in a group setting by trained nutritionists and each session includes information and activities that reflect both nutritional and behavioral principles. Participants also receive individual contacts and can participate in peer-led sessions to provide additional support and enhance adherence. Details of the intervention are published (13).

Dietary Assessment in the WHI Dietary Modification Trial

The primary dietary assessment instrument in the DM is the food frequency questionnaire. All participants completed an FFQ at baseline and Year 1. Thereafter, each woman completes an FFQ every 3 years for purposes of trial monitoring. The WHI FFQ was based on instruments previously used in the Women's Health Trial (14, 15) and the Women's Health Trial Feasibility Study in Minority Populations (16). WHI scientists modified the questionnaire to include additional questions on fat-related food preparation methods and reduced-fat foods to increase its sensitivity to changes in fat intake (17). The instrument also includes items reflecting regional and ethnic eating patterns throughout the United States. Information about the measurement characteristics of the WHI FFQ has been published (17).

In addition to the comprehensive FFQ assessment, randomly selected subsamples of participants complete food records and/or 24-hour dietary recalls each year to provide other types of dietary assessment data for monitoring DM adherence. Vitamin and mineral supplement use is assessed using a simplified inventory procedure. WHI participants bring their supplements to the clinic and trained non-nutritionists conduct the inventory at a computer station and directly enter data about multiple-vitamin(s) and single supplement(s), including dose, frequency, and duration of use. Details of this simplified supplement inventory procedure have been published (18).

Other Measures

At baseline, all DM participants completed extensive questionnaires about demographics, socioeconomic status, medical history, health-related behavior, psychosocial factors, and a 4-day food record. Details on the assessment of these items are given in the appendix to Anderson's article. During the screening clinic visits participants had physical and blood pressure measurements taken, breast examinations, electrocardiograms, and provided blood samples. Participants were asked to bring all medications to the clinic for entry into a medication inventory. Food records and blood samples were analyzed on a randomly selected subsample of these participants with over-sampling for minorities.

RESULTS

Similar to the presentation of results for the other components, the baseline description of participants in the Dietary Modification trial is stratified by age. Because there was a study-wide emphasis on inclusion of minorities, all demographic, medical history, dietary intake and blood analytes are given by race/ethnicity group in the Appendix to

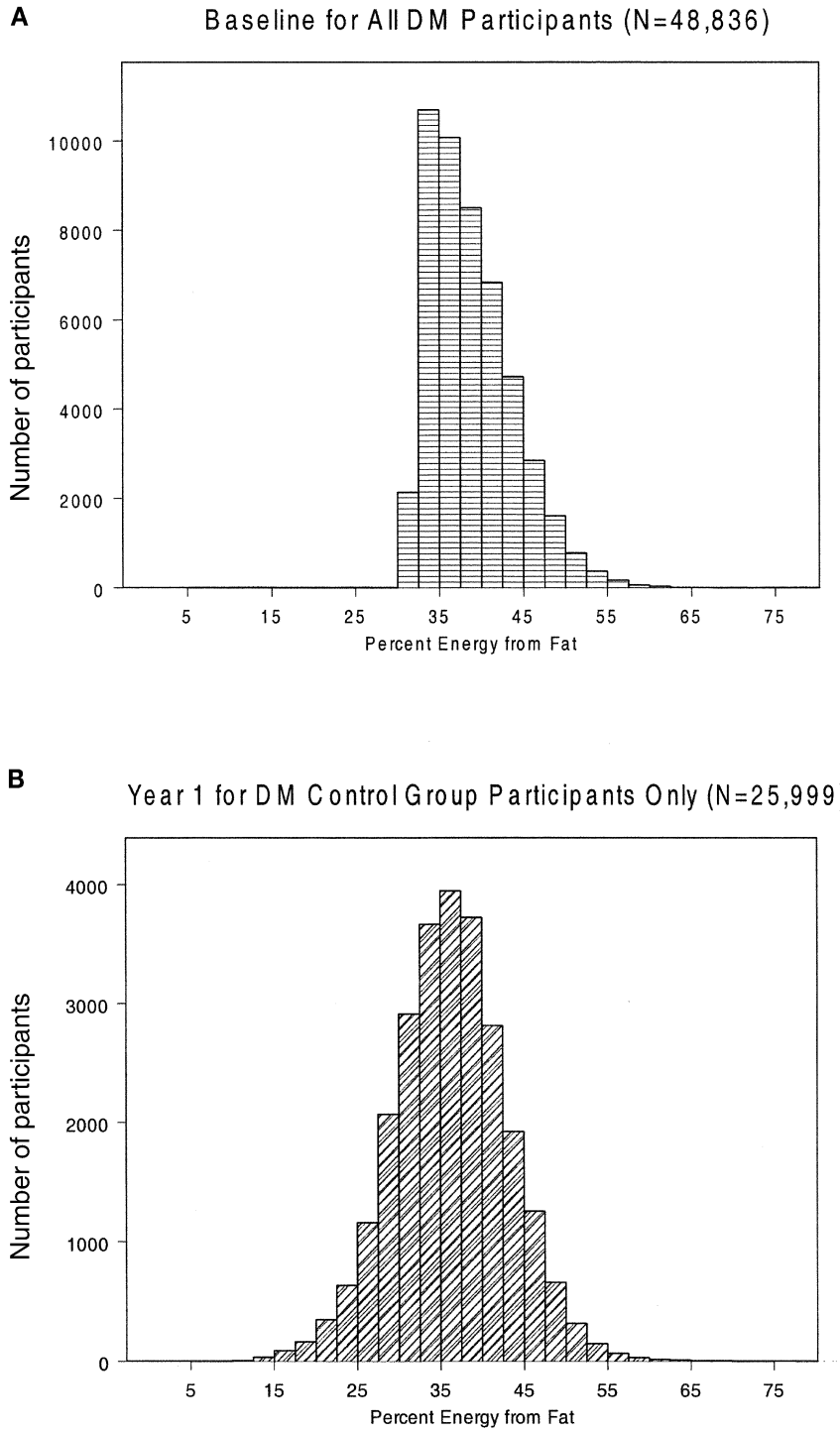

FIGURE 1. Distribution of percent energy from fat in WHI diet modification participants, as estimated by a food frequency questionnaire.

Hays' article. Differences by age and race/ethnicity are generally statistically significant because of the large sample sizes. Therefore, we simply present means, distributions, and differences, with emphasis on those factors that could be related to the clinical outcomes.

Participant Characteristics by Age (Table 1)

The age distributions (and design assumptions) are as follows: 37% (30%) of women were aged 50 to 59 years, 47% (45%) aged 60 to 69 years, and 17% (25%) aged 70 to 79 years, indicating lower than designed enrollment

TABLE 1. Baseline demographic and general health characteristics of WHI Dietary Modification participants by age

	Age at screening (y)											
	50–59 (N = 18,003)			60–69 (N = 22,713)			70–79 (N = 8120)			Total (N = 48,836)		
Characteristic	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD
Race/Ethnicity												
American Indian	89	0.5		91	0.4		23	0.3		203	0.4	
Asian/Pacific Islander	496	2.8		461	2.0		150	1.8		1107	2.3	
Black	2386	13.3		2267	10.0		613	7.5		5266	10.8	
Hispanic	972	5.4		739	3.3		143	1.8		1854	3.8	
White	13,806	76.7		18,877	83.1		7077	87.2		39,760	81.4	
Unknown	254	1.4		278	1.2		114	1.4		646	1.3	
Education												
0–8 years	188	1.1		279	1.2		109	1.3		576	1.2	
Some high school	440	2.5		813	3.6		386	4.8		1639	3.4	
High school diploma/GED	2463	13.8		4461	19.8		1594	19.7		8518	17.6	
School after high school	7083	39.6		8849	39.2		3376	41.8		19,308	39.8	
College degree or higher	7708	43.1		8168	36.2		2612	32.3		18,488	38.1	
Body mass index (BMI), kg/m^2												
Underweight (<18.5)	54	0.3		75	0.3		25	0.3		154	0.3	
Normal (18.5–24.9)	4826	27.0		5479	24.2		2198	27.2		12,503	25.7	
Overweight (25.0–29.9)	6032	33.7		8210	36.3		3145	38.9		17,387	35.8	
Obesity I (30.0–34.9)	4046	22.6		5308	23.5		1844	22.8		11,198	23.0	
Obesity II (35.0–39.9)	1961	11.0		2435	10.8		652	8.1		5048	10.4	
Obesity III (≥40)	988	5.5		1108	4.9		226	2.8		2322	4.8	
Height, (cm)	17,945		163.2 ± 6.5	22,647		162.0 ± 6.4	8093		160.0 ± 6.4	48,685		162.1 ± 6.5
Weight, (kg)	17,981		78.1 ± 17.4	22,696		77.1 ± 16.4	8118		72.9 ± 14.6	48,795		76.7 ± 16.6
Waist, (cm)	17,953		88.4 ± 14.3	22,657		89.7 ± 13.7	8101		88.7 ± 12.7	48,711		89.0 ± 13.8
Smoking												
Never smoked	8902	49.9		11498	51.2		4548	56.9		24,948	51.7	
Past smoker	7346	41.2		9610	42.8		3145	39.4		20,101	41.6	
Current smoker	1600	9.0		1356	6.0		294	3.7		3250	6.7	
Alcohol intake												
Never drinker	1494	8.4		2311	10.2		958	11.9		4763	9.8	
Past drinker	3106	17.4		4195	18.6		1599	19.9		8900	18.4	
Current drinker	13,279	74.3		16,065	71.2		5481	68.2		34,825	71.8	
Alcohol servings/wk for drinkers	16,367		2.3 ± 4.1	20,255		2.3 ± 4.1	7073		2.2 ± 4.0	43,695		2.3 ± 4.1
Physical activity												
No activity	3432	22.0		3919	18.9		1270	17.1		8621	19.7	
Some activity	6489	41.6		9221	44.4		3454	46.6		19,164	43.8	
2–<4 episodes/wk of moderate + activity	2668	17.1		3558	17.1		1297	17.5		7523	17.2	
4+ episodes/wk of moderate + activity	3015	19.3		4052	19.5		1387	18.7		8454	19.3	
Any supplement use												
No	7250	40.3		7546	33.2		2470	30.4		17,266	35.4	
Yes	10,753	59.7		15,167	66.8		5650	69.6		31,570	64.6	
Multivitamin use (with or without minerals)												
No	12,249	68.0		14,331	63.1		4917	60.6		31,497	64.5	
Yes	5754	32.0		8381	36.9		3203	39.4		17,338	35.5	

TABLE 2. Baseline medical history status of WHI Dietary Modification participants by age

	Age at screening (y)							
	50–59 (N = 18,003)		60–69 (N = 22,713)		70–79 (N = 8120)		Total (N = 48,836)	
Medical History	N	%	N	%	N	%	N	%
Age at first birth (y)[a]								
Never had term pregnancy	616	4.1	428	2.3	184	2.9	1228	3.0
<20	3152	21.0	3134	16.6	606	9.4	6892	17.1
20–29	10,034	66.9	13,924	73.7	4840	75.4	28,798	71.5
30+	1191	7.9	1401	7.4	788	12.3	3380	8.4
Age at menopause (y)								
<40	1674	10.0	2203	10.4	665	8.9	4542	10.0
40–49	7371	43.9	7788	36.8	2849	38.0	18,008	39.6
50+	7753	46.2	11,183	52.8	3978	53.1	22,914	50.4
Hysterectomy[b]								
No	10,627	59.0	12,606	55.5	4401	54.2	27,634	56.6
Yes	7376	41.0	10,107	44.5	3719	45.8	21,202	43.4
History of PHT use[c]								
Never	6225	34.6	9561	42.2	4023	49.6	19,809	40.6
Past	2059	11.5	3166	14.0	1540	19.0	6765	13.9
Current	9695	53.9	9949	43.9	2546	31.4	22,190	45.5
Total PHT duration among ever users (y)								
<5	6071	51.5	4118	31.3	1431	34.9	11,620	40.0
5–<10	3321	28.2	2703	20.6	528	12.9	6552	22.6
10–<15	1477	12.5	2721	20.7	487	11.9	4685	16.1
15+	909	7.7	3610	27.4	1651	40.3	6170	21.3
History of E-alone use[c]								
Never	11,613	64.6	13,950	61.5	4756	58.7	30,319	62.2
Past	1407	7.8	2701	11.9	1498	18.5	5606	11.5
Current	4967	27.6	6033	26.6	1853	22.9	12,853	26.3
Total E-alone duration among ever users (y)								
<5 (y)	3033	47.5	2879	32.9	1187	35.3	7099	38.3
5–<10 (y)	1687	26.4	1481	16.9	441	13.1	3609	19.5
10–<15 (y)	921	14.4	1555	17.7	396	11.8	2872	15.5
15+	749	11.7	2848	32.5	1340	39.8	4937	26.7
History of E + P use[c]								
Never	11,456	63.7	16,807	74.0	6969	85.9	35,232	72.2
Past	1689	9.4	1879	8.3	438	5.4	4006	8.2
Current	4844	26.9	4013	17.7	710	8.7	9567	19.6
Total E + P duration among ever users (y)								
<5 (y)	4208	64.3	2492	42.2	538	46.7	7238	53.2
5–<10 (y)	1779	27.2	1694	28.7	206	17.9	3679	27.0
10–<15 (y)	462	7.1	1207	20.4	177	15.4	1846	13.6
15+	97	1.5	513	8.7	230	20.0	840	6.2
Benign breast disease								
No	12,466	80.6	16,131	78.3	5775	78.5	34,372	79.1
Yes, 1 biopsy	2194	14.2	3218	15.6	1093	14.9	6505	15.0
Yes, 2+ biopsies	814	5.3	1255	6.1	492	6.7	2561	5.9
Family history of breast cancer								
No	14,257	82.8	17,627	82.0	6079	80.3	37,963	82.0
Yes	2955	17.2	3882	18.0	1488	19.7	8325	18.0
Systolic blood pressure (mm Hg)								
≤120	8716	48.4	7565	33.3	1817	22.4	18,098	37.1
>120–140	6985	38.8	9984	44.0	3561	43.9	20,530	42.0
>140	2301	12.8	5163	22.7	2742	33.8	10,206	20.9
Diastolic blood pressure (mm Hg)								
<90	16,442	91.3	21,097	92.9	7654	94.4	45,193	92.6
≥90	1561	8.7	1611	7.1	458	5.6	3630	7.4

(continued)

TABLE 2. *Continued*

	Age at screening (y)							
	50–59 (N = 18,003)		60–69 (N = 22,713)		70–79 (N = 8120)		Total (N = 48,836)	
Medical History	N	%	N	%	N	%	N	%
History of hypertension								
Never hypertensive	11,220	72.5	12,776	62.1	3985	54.5	27,981	64.5
Untreated hypertensive	1178	7.6	1723	8.4	602	8.2	3503	8.1
Treated hypertensive	3081	19.9	6071	29.5	2731	37.3	11,883	27.4
Treated diabetes (pills or shots)								
No	17,402	96.7	21,569	95.0	7658	94.3	46,629	95.5
Yes	599	3.3	1142	5.0	461	5.7	2202	4.5
Treated hypercholesterolemia (pills)								
No	14,158	92.4	17,675	86.3	6160	83.8	37,993	88.0
Yes	1172	7.6	2812	13.7	1188	16.2	5172	12.0
History of cardiovascular disease[d]								
No	16,689	93.6	19,973	89.0	6641	83.2	43,303	89.7
Yes	1143	6.4	2469	11.0	1338	16.8	4950	10.3
History of polyp removal								
No	14,530	94.7	18,462	90.7	6302	87.2	39,294	91.6
Yes	806	5.3	1889	9.3	926	12.8	3621	8.4
Family history of myocardial infarction								
No	9024	52.5	9787	45.5	3351	44.4	22,162	47.9
Yes	8155	47.5	11,709	54.5	4202	55.6	24,066	52.1
Family history of colorectal cancer								
No	14,358	86.1	17,248	83.0	5821	80.0	37,427	83.7
Yes	2309	13.9	3525	17.0	1451	20.0	7285	16.3
Parent broke bone after age 40								
No	10,002	60.1	12,405	59.3	4670	62.9	27,077	60.2
Yes	6635	39.9	8524	40.7	2749	37.1	17,908	39.8

PHT, postmenopausal hormone therapy; E-alone, estrogen alone; E+P, estrogen + progestin.
[a]Applies only to participants who have ever been pregnant.
[b]Hysterectomy at randomization.
[c]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.
[d]Includes MI, stroke, CHF, angina, carotid endarterectomy/angioplasty, DVT, PE, peripheral arterial disease, and CABG/PTCA.

of older women. Inclusion of a diverse population was successful with over 18% of participants belonging to a minority group. Overall, this appears to be a sample of healthy and health-conscious women, with high educational attainment (about 40% had college degrees), low rates of smoking (93% non-smokers), and high vitamin supplement use (65%). However, almost 40% of participants were obese with slightly lower rates in women aged 70 to 79 years.

In comparison to Whites, Blacks were more likely to be smokers, less likely to drink alcohol or engage in physical activity, and had higher body mass indices (BMI): 36% of Whites were obese compared with 58% of Blacks (appendix to Hays' article). Compared with Whites, Hispanics were generally younger, had lower educational attainment, and were somewhat more likely to be obese. Asian/Pacific Islanders had highest levels of education and were least likely to drink, smoke, or be obese. American Indians were similar to Whites in smoking, exercise, and alcohol consumption; but had lower education levels and higher obesity levels (51% were obese compared with 36% of Whites). Whites and Asian/Pacific Islanders were more likely to use dietary supplements than other race/ethnicity groups.

Medical History Variables (Table 2)

Prevalence of potential risk factors for breast cancer, colorectal cancer, and cardiovascular events by age are given in Table 2. In relation to breast cancer risk, only a few variables showed differences by age. A greater percentage of older women were over the age of 30 before having their first birth and had never used hormone replacement therapy. As would be expected, a greater percentage of older women reported treatment for hypertension, diabetes, and high blood cholesterol levels as well as history of cardiovascular disease and polyp removal.

Compared with White participants, Blacks were more likely to have been less than 20 years of age at first birth (15% vs. 35%, respectively), less likely to be taking hormone replacement therapy (48% vs. 27%), and more likely to be treated for hypertension (25% vs. 46%) or diabetes (3% vs. 12%) (appendix to Hays' article). Compared with

TABLE 3. Dietary intake of WHI Dietary Modification control participants by age, from a Food Frequency Questionnaire[a]

	Age at screening (y)							
	50–59 (N = 9360)		60–69 (N = 12,235)		70–79 (N = 4404)		Total (N = 25,999)	
Nutrient[b]	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD
Energy (kcal)		1528 ± 566		1501 ± 541		1476 ± 534		1506 ± 549
Total fat (g)		60 ± 27		60 ± 26		58 ± 25		60 ± 26
% Energy from fat		35 ± 7		36 ± 7		36 ± 6		36 ± 7
% Energy from carbohydrates		46 ± 8		46 ± 8		47 ± 8		46 ± 8
% Energy from protein		17 ± 3		17 ± 3		16 ± 3		17 ± 3
Total PFA (g)		12 ± 6		12 ± 5		12 ± 5		12 ± 5
Total MFA (g)		22 ± 10		22 ± 9		22 ± 9		22 ± 10
Total SFA (g)		21 ± 10		20 ± 9		20 ± 9		20 ± 9
Total trans fatty acid (g)		3.6 ± 1.5		3.6 ± 1.5		3.6 ± 1.6		3.6 ± 1.5
Animal protein (g)		44 ± 20		44 ± 19		42 ± 19		44 ± 20
Vegetable protein (g)		17 ± 7		17 ± 7		17 ± 7		17 ± 7
Dietary fiber (g)		14 ± 6		15 ± 6		15 ± 6		14 ± 6
Cholesterol (mg/1000 kcal)		135 ± 47		135 ± 48		134 ± 49		135 ± 48
Total vitamin A (mcg Re)		7158 ± 3785		7807 ± 3994		8362 ± 4213		7655 ± 3977
Total alpha-toc eq (mg)		7.8 ± 3.1		7.9 ± 3.1		7.9 ± 3.1		7.9 ± 3.1
Vitamin C (mg)		85 ± 47		91 ± 49		97 ± 50		90 ± 49
Roboflavin (mg)		1.5 ± 0.4		1.6 ± 0.4		1.6 ± 0.4		1.6 ± 0.4
Niacin (mg)		16 ± 6		16 ± 5		16 ± 6		16 ± 6
Vitamin B6 (mg)		1.5 ± 0.4		1.5 ± 0.4		1.6 ± 0.4		1.5 ± 0.4
Folacin (mcg)		210 ± 87		221 ± 88		226 ± 89		218 ± 88
Vitamin B12 (mcg)		4.9 ± 2.2		4.9 ± 2.2		4.8 ± 2.2		4.9 ± 2.2
Calcium (mg)		642 ± 339		641 ± 331		651 ± 338		643 ± 335
Magnesium (mg)		233 ± 88		236 ± 87		235 ± 87		235 ± 87
Iron (mg)		12 ± 5		12 ± 5		12 ± 5		12 ± 5
Zinc (mg)		9.7 ± 3.8		9.6 ± 3.8		9.4 ± 3.7		9.6 ± 3.8
Total carotenoids (mcg)		11,990 ± 6300		12,100 ± 6158		12,122 ± 6190		12,064 ± 6215
Beta-carotene (mcg)		2832 ± 1763		3127 ± 1882		3380 ± 1990		3057 ± 1866
Lycopene (mcg)		6444 ± 4193		6138 ± 3958		5795 ± 3806		6186 ± 4020
Lutein + zeaxanthin (mcg)		1317 ± 692		1360 ± 724		1394 ± 750		1350 ± 717
	(N = 9605)		(N = 12,544)		(N = 4514)		(N = 26,663)	
Fruits and vegetables (servings/day)		3.1 ± 1.2		3.4 ± 1.3		3.6 ± 1.4		3.3 ± 1.3
0 to <3	47.9		40.3		35.3		42.2	
3 to <5	34.9		38.4		38.9		37.3	
5+	17.2		21.2		25.8		20.5	
Grains (servings/day)		4.5 ± 1.9		4.2 ± 1.7		3.9 ± 1.6		4.3 ± 1.8

[a]Year 1 control participant data are presented to represent baseline intake. Baseline dietary data are biased because of eligibility screening (i.e., women with fat intakes less than 32% energy from fat were ineligible for the Diet Modification trial).
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

Whites, Hispanic women were more likely to have been less than 20 years of age at first birth (15% vs. 24%, respectively), less likely to be taking hormone replacement therapy (48% vs. 39%), and more likely to be treated for diabetes (3% vs. 6%). Asian/Pacific Islanders tended to be similar to Whites on these variables. However, compared with Whites, they were more likely to be treated for hypertension (25% vs. 31%, respectively), diabetes (3% vs. 6%), or taking cholesterol lowering drugs (12% vs. 18%). Compared with Whites, American Indians were more likely to have been less than 20 years of age at first birth (15% vs. 31%, respectively), less likely to be taking hormone replacement therapy (48% vs. 38%, respectively), more likely to be treated for diabetes (3% vs. 6%) and hypertension (25% vs. 32%) and more likely to have a family history of heart disease (10% vs. 15%, respectively).

Dietary Intake Estimates (from Food Only) by Age (Table 3) and Race Ethnicity (Table 4)

Although Table 3 gives data on an extensive list of nutrients, the narrative here is focused on nutrients related to the dietary intervention aims of the trial. Mean energy intake estimates were about 1500 kcals per day, energy from fat was 36%, and dietary fiber intake was 14 grams per day. There was little variability by age. Participants consumed

TABLE 4. Dietary intake of WHI Dietary Modification control participants by race/ethnicity, from a Food Frequency Questionnaire[a]

	Race/Ethnicity											
	American Indian (N = 94)		Asian/Pacific Islander (N = 611)		Black (N = 2447)		Hispanic (N = 870)		White (N = 21,643)		Total[b] (N = 25,999)		
Nutrient[c]	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	%	Mean ± SD	N	%	Mean ± SD
Energy (kcal)		1430 ± 546		1450 ± 550		1411 ± 582		1456 ± 604		1523 ± 540	21,943		1506 ± 549
Total Fat (g)		59 ± 27		58 ± 27		57 ± 28		57 ± 29		60 ± 26	21,943		60 ± 26
% Energy from fat		37 ± 8		36 ± 7		36 ± 7		35 ± 7		36 ± 7	21,943		36 ± 7
% Energy from carbohydrates		45 ± 9		48 ± 8		47 ± 9		47 ± 9		46 ± 8	21,943		46 ± 8
% Energy from protein		16 ± 3		16 ± 3		16 ± 3		16 ± 3		17 ± 3	21,943		17 ± 3
Total PFA (g)		12 ± 5		13 ± 6		12 ± 6		12 ± 6		12 ± 5	21,943		12 ± 6
Total MFA (g)		22 ± 10		22 ± 10		22 ± 10		22 ± 11		22 ± 9	21,943		22 ± 10
Total SFA (g)		20 ± 10		18 ± 9		19 ± 9		19 ± 10		21 ± 9	21,943		20 ± 9
Total trans fatty acid (g)		3.4 ± 1.3		3.1 ± 1.3		3.9 ± 1.8		3.0 ± 1.4		3.6 ± 1.5	21,943		3.6 ± 1.5
Animal protein (g)		40 ± 18		38 ± 20		38 ± 20		41 ± 21		45 ± 19	21,943		44 ± 20
Vegetable protein (g)		17 ± 8		19 ± 8		16 ± 7		17 ± 8		18 ± 7	21,943		17 ± 7
Dietary fiber (g)		14 ± 6		13 ± 5		13 ± 5		14 ± 6		15 ± 6	21,943		15 ± 6
Cholesterol (mg/1000 kcal)		146 ± 59		139 ± 49		142 ± 57		143 ± 54		133 ± 47	21,943		135 ± 48
Total Vitamin A (mcg Re)		6706 ± 3710		7745 ± 4307		7245 ± 4288		6016 ± 3490		7787 ± 3918	21,943		7655 ± 3977
Total Alpha-Toc Eq (mg)		7.3 ± 2.6		8.0 ± 3.1		7.4 ± 3.1		7.2 ± 3.1		8.0 ± 3.1	21,943		7.9 ± 3.1
Vitamin C (mg)		82 ± 47		83 ± 48		84 ± 51		80 ± 48		91 ± 48	21,943		90 ± 49
Riboflavin (mg)		1.4 ± 0.3		1.3 ± 0.3		1.3 ± 0.4		1.4 ± 0.4		1.6 ± 0.4	21,943		1.6 ± 0.4
Niacin (mg)		15 ± 6		16 ± 6		15 ± 6		15 ± 6		17 ± 6	21,943		16 ± 6
Vitamin B6 (mg)		1.4 ± 0.3		1.4 ± 0.3		1.3 ± 0.3		1.4 ± 0.4		1.6 ± 0.4	21,943		1.5 ± 0.4
Folacin (mcg)		203 ± 82		197 ± 83		192 ± 87		187 ± 83		223 ± 87	21,943		218 ± 88
Vitamin B12 (mcg)		4.6 ± 2		4.8 ± 241		5.3 ± 2.9		4.4 ± 2.2		4.9 ± 2.1	21,943		4.9 ± 2.2
Calcium (mg)		556 ± 285		467 ± 241		478 ± 257		609 ± 337		674 ± 338	21,943		643 ± 335
Magnesium (mg)		223 ± 85		214 ± 80		198 ± 84		213 ± 87		241 ± 86	21,943		235 ± 87
Iron (mg)		11 ± 4		11 ± 4		11 ± 5		11 ± 5		12 ± 5	21,943		12 ± 5
Zinc (mg)		8.6 ± 3.3		8.8 ± 3.7		8.1 ± 3.5		8.7 ± 3.8		9.9 ± 3.7	21,943		9.6 ± 3.8
Total carotenoids (mcg)		11,625 ± 6275		11,314 ± 6035		10,087 ± 5949		10,320 ± 6145		12,423 ± 6164	21,943		12,064 ± 6215
Beta-carotene (mcg)		2662 ± 1810		3434 ± 2114		2944 ± 2000		2351 ± 1594		3097 ± 1844	21,943		3057 ± 1866
Lycopene (mcg)		6332 ± 3938		4747 ± 3296		4322 ± 3349		5551 ± 4326		6524 ± 3988	21,943		6186 ± 4020
Lutein + Zeaxanthin (mcg)		1306 ± 794		1501 ± 876		1494 ± 916		1172 ± 669		1339 ± 689	21,943		1350 ± 717
		(N = 97)		(N = 628)		(N = 2615)		(N = 918)		(N = 22,059)			(N = 26,663)
Fruits and vegetables (servings/day)		2.8 ± 1.1		3.0 ± 1.2		2.9 ± 1.2		2.6 ± 1.1		3.4 ± 1.3	26,657		3.3 ± 1.3
0 to <3	52.6		50.5		54.1		61.2		39.6		11,254	42.2	
3 to <5	34.0		33.4		30.5		25.2		38.8		9931	37.3	
5+	13.4		16.1		15.4		13.6		21.6		5472	20.5	
Grains (servings/day)		3.9 ± 1.7		4.4 ± 1.7		3.8 ± 1.8		4.9 ± 2.4		4.3 ± 1.7	26,656		4.3 ± 1.8

[a]Year 1 control participant data are presented to represent baseline intake. Beseline dietary data are biased because of eligibility screening (i.e., women with fat intakes less than 32% energy from fat were ineligible for the Diet Modification trial).
[b]Total includes Unknown race/ethnicity.
[c]Means and standard deviations were computed on the log scale and back-transformed values are reported.

approximately three servings of fruits and vegetables per day and only 20% met the recommendation to consume five or more servings per day. Older women were more likely to meet this recommendation, with 26% of women aged 70 to 79 years consuming five a day compared with only 17% among women aged 50 to 59 years. Average grain servings per day was four. Average daily dietary calcium intake was only 640 mg.

Among White participants, average daily energy intake was about 1500 kcals (Table 4). Minority women reported somewhat lower levels (1410–1450 kcals). Mean energy from fat was 36% with little variation by race/ethnicity. Twenty-two percent of Whites met the recommendation to consume five or more fruits and vegetables per day compared with only fourteen to sixteen percent among the minority groups. Hispanics reported consuming the most servings of grains. There were marked differences in calcium intakes: Whites consumed almost 700 mg per day compared with only 500 to 600 mg among the minority groups.

Blood Analytes by Race/Ethnicity (Appendix to Hays' article)

Total serum cholesterol was about 220 mg/dl and varied only slightly by race/ethnicity. Lp(a) was 2-fold higher in Blacks compared with other race/ethnicity groups. Triglycerides were notably lower in Blacks (143 mg/dl) compared with other groups (about 150 mg/dl). Compared with Whites, glucose was higher in Blacks and American Indians and serum insulin levels were somewhat higher for Blacks, Hispanics, and American Indians. There was no consistent pattern of variability in concentrations of carotenoids by race/ethnicity.

DISCUSSION

Comparisons of Key Variables to National Data

Since DM participants were not recruited as a representative sample from the US population, it is instructive to compare this sample to US women aged 50 to 79 years. Compared with women from the NHANES III, DM participants are more obese. Specifically, in the three age decades, 73%, 76%, and 73% of DM participants have BMI greater than 25 as compared with 64%, 64%, and 58% of NHANES III women (19). In contrast, DM participants have lower rates of hypertension: 28%, 38%, and 45% compared with 27%, 47%, and 57% in the NCHS study sample (20). DM participants are also much less likely to be current smokers than older US women. For example, 22% of women aged 55 to 64 years in the US currently smoke as measured by the Behavioral Risk Factor Surveillance Survey (21) compared with 9% of women aged 50 to 59 years and 6% of women aged 60 to 69 years in the DM.

Mean energy intakes for DM women were lower than those estimated from 24-hour recalls in NHANES III (22). For example, NHANES III values for women aged 60 to 69 years were 1578 kcals compared with 1506 kcals in WHI. This may be due, in part, to the different dietary assessment methods. In general, FFQs appear to underestimate energy intake compared with 24-hour recalls or diet records (23) more among women (24–27) and among Blacks compared with Whites (28). The latter bias may partially explain differences in energy intake by ethnicity in WHI.

A substudy comparing the WHI FFQ to food records and recalls also suggested that there was underreporting of energy intake from the FFQ (17). This study of 113 DM participants found that the FFQ under-estimated energy intake by 100 to 130 kcals and provided an unbiased estimate of absolute fat intake in grams, such that the percentage energy from fat estimated from the FFQ was biased upward from the recall estimate by approximately three percentage points. Precision of the FFQ was good as evidenced by a correlation coefficient of 0.6 for percentage energy from fat estimated by the FFQ compared with the criterion measure (8 days of food records and recalls). Nonetheless, it is clear from studies of doubly-labeled water that energy intake is underestimated in all self-report methods of assessing dietary intake (23, 29, 30) and some research suggests that fat may be differentially underreported (31). In addition, many person-specific biases have been identified, including underreporting associated with obesity (32, 33), social desirability (34), and dietary interventions themselves (35). Therefore, although the collection of dietary data is useful for monitoring trial performance and may provide valuable information for addressing secondary hypotheses about diet and disease risk, the randomized nature of the DM trial is its chief strength.

Comparison of the WHI Dietary Modification Trial Component to Other Dietary Intervention Trials

There are several large ongoing, or recently completed, dietary interventions for prevention of cancer or cardiovascular disease (36–41). WHI is unique among them in that it combines all the following design elements: the intervention is a dietary pattern and thus intervenes on multiple nutrients simultaneously; the duration of the intervention is longer than most (average 8.5 years) and should be adequate to observe hypothesized health outcomes; there are multiple endpoints (both cancer and cardiovascular) that focus on disease occurrence rather than risk factors or intermediate outcomes; and finally, it is a primary rather than secondary prevention trial. These features are particularly noteworthy given the recent null results of two dietary intervention trials (one of a low-fat high-fiber diet and one of fiber supplements) on the recurrence of colorectal adenomas (36,

37), where it was noted that the results of these short-terms trials do not provide definitive answers to questions regarding diet and colorectal cancer risk (42).

Given the considerable limitations of observational epidemiologic studies and short term clinical trials, the randomized controlled Dietary Modification trial will provide a new and much needed line of evidence for resolving the important public health question of whether older women, by changing to a low-fat dietary pattern, can lower their risk of breast cancer, colon cancer, and heart disease.

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ELSEVIER

The Women's Health Initiative Calcium–Vitamin D Trial: Overview and Baseline Characteristics of Participants

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INTRODUCTION

Osteoporosis is a major public health issue leading to significant morbidity, loss of independence and excess loss of life. It has been estimated that 13 to 17 million postmenopausal women have low bone mass or osteoporosis (1, 2). This is associated with almost 1.5 million fractures annually, including 300,000 hip fractures (2, 3). A review of the evidence by Cumming in 1990 (4) and subsequently published randomized clinical trials have shown that calcium and/or vitamin D supplements may play a role in the prevention and treatment of osteoporosis by slowing the rates of bone loss in postmenopausal and elderly women (5–9). However, there are a limited number of calcium and/or vitamin D trials (10–13) and observational studies [review of evidence by Cumming and Nevitt (14) and Kanis (15)], to support a role for calcium and vitamin D supplementation in the reduction of hip and other fractures. It has also been suggested that calcium and vitamin D supplementation may play a role in the reduction of colorectal cancer incidence (16–21). To address these major health concerns of postmenopausal women, the Calcium-Vitamin D (CaD) trial of the Women's Health Initiative (WHI) was designed to test the primary hypothesis that women who are randomized to receive calcium and vitamin D supplementation will have a lower risk of hip fracture and secondarily, a lower risk of all fractures and colorectal cancer than women receiving corresponding placebo. The objective of this paper is to describe the 36,282 women enrolled in the WHI CaD trial cohort with an emphasis on risk factors for osteoporotic fracture and colorectal cancer.

METHODS

Enrollment of Study Participants

Enrollment into the CaD component was delayed by one year to avoid undue participant burden at entry into WHI. Participants in the Diet Modification (DM) and/or Postmenopausal Hormone Therapy (PHT) component(s) were invited to join the CaD trial at the first or second annual follow-up visit (see Anderson's article and Hays' article in this issue for details of the design, recruitment, and screening process). Informed consent was obtained at the CaD randomization visit. The Institutional Review Boards at each of the participating institutions approved the CaD protocol.

Eligibility Criteria

Only women who were already randomized into another component of the WHI clinical trial were eligible to join CaD. Women were allowed to continue their own personal use of calcium and vitamin D as long as their personal vitamin D intake did not exceed 600 IU. The upper limit of personal Vitamin D intake was raised to 1000 IU after the Institute of Medicine released the report on safe upper limits of calcium and vitamin D intake (22). Eligibility criteria for the CaD component of the clinical trials are noted in Table 1 of Hays' article in this issue.

Study Medication

Willing and eligible women were randomly assigned in a double blind fashion to supplement or placebo. Each active tablet consisted of 500 mg of elemental calcium (as calcium carbonate) and 200 IU of Vitamin D_3. Participants were

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instructed to take two tablets per day (either active supplement or matching placebo), preferably in divided doses, with meals. This regimen was chosen to maximize absorption of the calcium. Initially, only a chewable formulation was available but in October 1997, in an effort to enhance tolerability, a swallowable form of the CaD supplement and placebo was developed and made available. A visual inspection of the CaD study pills was provided and a taste and/or swallow test was offered before randomization. At each annual visit, women already enrolled in CaD are given the option of switching to the other formulation if desired.

Data Collection and Definition of Variables

Demographic and medical history data were obtained by self-report using standardized questionnaires. Physical measurements, including blood pressure, height and weight, and blood samples were taken by certified staff at the clinic visit following standardized written procedures. Details of data definitions can be found in appendix to Anderson's article.

Bone Mineral Density

Bone mineral density (BMD) was measured by fan-beam Dual energy X-Ray Absorptiometry (DXA) at three WHI clinical centers (Alabama, Arizona, and Pittsburgh) using either the QDR 2000, 2000+, or 4500 (Hologic, Inc., Waltham, MA). Total hip, antero-posterior lumbar spine and whole body BMD and body composition were measured in all WHI participants at entry into WHI (baseline for PHT and DM) at these three WHI clinical centers. This resulted in a total of 2,529 women in the CaD bone density cohort (6.9%). The DXA measurements are repeated at year one (baseline for CaD) and years three, six, and nine. A standardized procedure for participant positioning and scan analysis was executed for all scans. All DXA operators attended a central training session and were certified on the basis of an evaluation of scanning and analysis technique. Densitometry technicians at the DXA coordinating center (University of California, San Francisco) reviewed a random sample of all scans, scans with exceptionally high or low BMD, and problematic scans flagged at the clinic, to assure adherence to standardized analysis techniques. The review comments were then returned to the clinics where any re-analyses or re-scanning was performed.

The DXA quality assurance (QA) program included clinic and coordinating center monitoring of scanner performance based on phantom scanning, and hardware/software change control. Spine phantoms were scanned daily and hip phantoms once per week. In March 2000, an experimental whole body phantom was developed and incorporated into the WHI BMD QA program. The whole body phantom was scanned three times per week. The data were plotted and reviewed for uncharacteristic surges or drifts indicating possible changes in scanner calibration. When possible problems were detected, the phantom data were analyzed using the CUSUM quality control method (23). Problems with the periodic air and tissue bar scanning were referred to the Hologic service department. Hardware/software change control consisted of both in-vitro and in-vivo cross-calibration.

RESULTS

Because the focus of the CaD trial is on hip and all fractures and colorectal cancer, the results presented below focus on the baseline characteristics of the CaD cohort that are likely to affect risk of these outcomes. Data presented reflect the characteristics of the CaD trial cohort at entry into the WHI clinical trial at baseline unless otherwise noted.

Demographic Characteristics of CaD Trial Participants (Table 1)

A total of 36,282 WHI participants were randomized into the CaD trial. The majority of these women (86.2%) were enrolled in only one of the other WHI trials: 20,193 (55.7%) in the DM trial and 11,072 (30.5%) in the PHT trial. The remaining 5,017 (13.8%) women were enrolled in both of the other two WHI trials. The mean age of the CaD trial cohort was 62.4 years (±6.9 years) with 37.0% aged 50 to 59 years, 45.5% aged 60 to 69 years, and 17.5% aged 70 years and older. This differs from the original design of the CaD trial, which assumed fewer women aged 50 to 59 years (30%) and more women aged 70 years and older (25%). Overall, 83.1% of women enrolled in the CaD trial were non-Hispanic White, 9.1% were Black, 4.2% were Hispanic, 2% were Asian/Pacific Islander, 0.4% were American Indian, and 1.2% were of unknown racial/ethnic origin. The percentage of minority participants was greatest among women in their fifties (22%).

Risk Factors for Hip Fracture and Other Medical History Characteristics (Tables 1 and 2)

The average body mass index of CaD trial participants was 29.0 kg/M^2. Few women (0.4%) in the CaD trial had body mass index <18.5, whereas 37.6% had body mass index ≥ 30. Body weight was ≤ 57.8 kgs for 9.3% of White participants, 3.4% of Black participants, and 10.8% of Hispanic women (the appendix to Hays' article).

Overall, 7.7% of women were current smokers with smoking most common among women in their fifties (10.4%), and least common among women in their seventies (3.8%) (Table 1). Three-fourths of women reported at least some weekly moderate or strenuous physical activity with one in

TABLE 1. Baseline demographic and general health characteristics of WHI Calcium and Vitamin D participants by age

	Age at screening (y)											
	50–59 (N = 13,422)			60–69 (N = 16,520)			70–79 (N = 6340)			Total (N = 36,282)		
Characteristic	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD
Race/Ethnicity												
American Indian	61	0.5		68	0.4		20	0.3		149	0.4	
Asian/Pacific Islander	309	2.3		301	1.8		112	1.8		722	2.0	
Black	1572	11.7		1354	8.2		391	6.2		3317	9.1	
Hispanic	844	6.3		546	3.3		117	1.8		1507	4.2	
White	10,469	78.0		14,057	85.1		5627	88.8		30,153	83.1	
Unknown	167	1.2		194	1.2		73	1.2		434	1.2	
Education												
0–8 years	209	1.6		233	1.4		85	1.3		527	1.5	
Some high school	399	3.0		659	4.0		317	5.0		1375	3.8	
High school diploma/GED	2056	15.4		3400	20.7		1217	19.3		6673	18.5	
School after high school	5262	39.5		6510	39.6		2600	41.2		14,372	39.9	
College degree or higher	5385	40.5		5620	34.2		2093	33.2		13,098	36.3	
Body mass index (BMI), kg/m^2	13,345		29.3 ± 6.2	16,438		29.2 ± 5.9	6312		28.2 ± 5.3	36,095		29.0 ± 5.9
Underweight (<18.5)	48	0.4		64	0.4		36	0.6		148	0.4	
Normal (18.5–24.9)	3551	26.6		4065	24.7		1814	28.7		9430	26.1	
Overweight (25.0–29.9)	4497	33.7		6016	36.6		2442	38.7		12,955	35.9	
Obesity I (30.0–34.9)	3006	22.5		3813	23.2		1384	21.9		8203	22.7	
Obesity II (35.0–39.9)	1460	10.9		1698	10.3		486	7.7		3644	10.1	
Obesity III (≥40)	783	5.9		782	4.8		150	2.4		1715	4.8	
Waist/hip ratio (WHR)	13,372		0.81 ± 0.1	16,461		0.82 ± 0.1	6316		0.83 ± 0.1	36,149		0.82 ± 0.1
Waist (cm)	13,383		88.5 ± 14.3	16,475		89.4 ± 13.6	6321		88.2 ± 12.6	36,179		88.9 ± 13.7
Smoking												
Never smoked	6614	49.7		8505	52.0		3634	58.1		18,753	52.2	
Past smoker	5304	39.9		6701	41.0		2383	38.1		14,388	40.1	
Current smoker	1384	10.4		1141	7.0		236	3.8		2761	7.7	
Alcohol intake												
Never drinker	1164	8.7		1794	10.9		796	12.7		3754	10.4	
Past drinker	2282	17.1		2903	17.7		1216	19.3		6401	17.8	
<1 drink per mo	2018	15.1		2260	13.8		771	12.3		5049	14.0	
<1 drink per wk	2906	21.8		3407	20.8		1308	20.8		7621	21.2	
1–<7 drinks per wk	3590	26.9		4317	26.3		1482	23.6		9389	26.1	
7+ drinks per wk	1370	10.3		1724	10.5		716	11.4		3810	10.6	
Physical activity												
No activity	2559	21.5		2804	18.4		961	16.3		6324	19.2	
Some activity	4938	41.5		6692	44.0		2682	45.5		14,312	43.4	
2–<4 episodes/wk of moderate + activity	1955	16.4		2530	16.6		1049	17.8		5534	16.8	
4+ episodes per wk of moderate + activity	2443	20.5		3175	20.9		1206	20.4		6824	20.7	
Multivitamin use (with or without minerals)												
No	9129	68.0		10,359	62.7		3866	61.0		23,354	64.4	
Yes	4292	32.0		6161	37.3		2474	39.0		12,927	35.6	
Vitamin C as single supplement												
No	10,791	80.4		12,555	76.0		4748	74.9		28,094	77.4	
Yes	2631	19.6		3965	24.0		1592	25.1		8188	22.6	
Vitamin E as single supplement												
No	10,625	79.2		12,038	72.9		4561	71.9		27,224	75.0	
Yes	2797	20.8		4482	27.1		1779	28.1		9058	25.0	
Calcium as single supplement (including antacids)												
No	10,557	78.7		12,469	75.5		4600	72.6		27,626	76.1	
Yes	2865	21.3		4051	24.5		1740	27.4		8656	23.9	
Single supplement (not Vit C, E, or calcium)												
No	9308	69.3		10,779	65.2		4060	64.0		24,147	66.6	
Yes	4114	30.7		5741	34.8		2280	36.0		12,135	33.4	

TABLE 2. Baseline medical history status of WHI Calcium and Vitamin D participants by age

	Age at screening (y)							
	50–59 (N = 13,422)		60–69 (N = 16,520)		70–79 (N = 6340)		Total (N = 36,282)	
Medical History	N	%	N	%	N	%	N	%
Hysterectomy[a]								
No	8062	60.1	9544	57.8	3556	56.1	21,162	58.3
Yes	5360	39.9	6976	42.2	2784	43.9	15,120	41.7
Age at first birth (y)[b]								
Never had term pregnancy	419	3.7	296	2.1	131	2.6	846	2.8
<20	2527	22.4	2451	17.7	505	9.9	5483	18.1
20–29	7470	66.4	10,121	73.1	3830	75.0	21,421	70.9
30+	841	7.5	986	7.1	639	12.5	2466	8.2
Age last had any menstrual bleeding (y)								
<40	1917	17.5	1960	13.6	524	9.4	4401	14.2
40–44	1438	13.1	2049	14.2	789	14.2	4276	13.8
45–49	2438	22.2	3067	21.3	1302	23.4	6807	22.0
50–54	4059	37.0	4560	31.7	1962	35.3	10,581	34.2
55–60	1124	10.2	1912	13.3	688	12.4	3724	12.0
60+			843	5.9	293	5.3	1136	3.7
History of PHT use[c]								
Never	5549	41.4	8046	48.8	3565	56.3	17,160	47.4
Past	1902	14.2	2826	17.1	1396	22.0	6124	16.9
Current	5956	44.4	5625	34.1	1375	21.7	12,956	35.8
Total PHT duration (y)								
Non-user	5549	41.3	8046	48.7	3565	56.2	17,160	47.3
<5	4252	31.7	3131	19.0	1119	17.6	8502	23.4
5–<10	2163	16.1	1724	10.4	403	6.4	4290	11.8
10–<15	903	6.7	1605	9.7	338	5.3	2846	7.8
15+	555	4.1	2014	12.2	915	14.4	3484	9.6
History of E-alone use[c]								
Never	9084	67.7	10,817	65.5	4008	63.2	23,909	66.0
Past	1281	9.5	2308	14.0	1326	20.9	4915	13.6
Current	3049	22.7	3378	20.5	1000	15.8	7427	20.5
Total E-alone duration (y)								
Non-user	9084	67.7	10,817	65.5	4008	63.2	23,909	65.9
<5	2179	16.2	2254	13.6	969	15.3	5402	14.9
5–<10	1121	8.4	932	5.6	343	5.4	2396	6.6
10–<15	568	4.2	931	5.6	278	4.4	1777	4.9
15+	470	3.5	1586	9.6	742	11.7	2798	7.7
History of E + P use[c]								
Never	9136	68.1	12,814	77.6	5656	89.2	27,606	76.1
Past	1303	9.7	1401	8.5	299	4.7	3003	8.3
Current	2973	22.2	2295	13.9	383	6.0	5651	15.6
Total E + P duration (y)								
Non-user	9136	68.1	12,814	77.6	5656	89.2	27,606	76.1
<5	2834	21.1	1688	10.2	329	5.2	4851	13.4
5–<10	1128	8.4	1035	6.3	132	2.1	2295	6.3
10–<15	274	2.0	702	4.2	96	1.5	1072	3.0
15+	50	0.4	281	1.7	127	2.0	458	1.3
Family history of myocardial infraction								
No	6762	52.7	7184	45.8	2639	44.5	16,585	48.2
Yes	6063	47.3	8493	54.2	3294	55.5	17,850	51.8
Family history of breast cancer								
No	10,637	83.0	12,882	82.4	4807	81.1	28,326	82.4
Yes	2177	17.0	2743	17.6	1123	18.9	6043	17.6
Family history of colorectal cancer								
No	10,738	86.5	12,469	82.7	4599	80.5	27,806	83.8
Yes	1671	13.5	2605	17.3	1112	19.5	5388	16.2

(*continued*)

TABLE 2. *Continued*

	Age at screening (y)							
	50–59 (N = 13,422)		60–69 (N = 16,520)		70–79 (N = 6340)		Total (N = 36,282)	
Medical History	N	%	N	%	N	%	N	%
Parent broke bone after age 40								
No	7362	59.5	8991	58.8	3602	62.0	19,955	59.6
Yes	5013	40.5	6307	41.2	2207	38.0	13,527	40.4
Systolic blood pressure (mm Hg)								
⩽120	6520	48.6	5586	33.8	1486	23.4	13,592	37.5
120–140	5239	39.0	7304	44.2	2727	43.0	15,270	42.1
>140	1663	12.4	3630	22.0	2127	33.5	7420	20.5
Diastolic blood pressure (mm Hg)								
<90	12,263	91.4	15,350	92.9	5972	94.2	33,585	92.6
⩾90	1159	8.6	1166	7.1	366	5.8	2691	7.4
Hypertension								
Never hypertensive	8772	74.3	9696	64.3	3305	56.9	21,773	66.6
Untreated hypertensive	926	7.8	1235	8.2	483	8.3	2644	8.1
Treated hypertensive	2112	17.9	4143	27.5	2024	34.8	8279	25.3
Treated diabetes (pills or shots)								
No	12,958	96.6	15740	95.3	5987	94.6	34,685	95.6
Yes	461	3.4	775	4.7	345	5.4	1581	4.4
Treated hypercholesterolemia (pills)								
No	10,797	92.4	12,925	86.1	4827	82.7	28,549	87.8
Yes	884	7.6	2079	13.9	1009	17.3	3972	12.2
Benign breast disease								
No	9638	81.7	12,003	79.6	4621	79.0	26,262	80.2
Yes, 1 biopsy	1598	13.6	2235	14.8	867	14.8	4700	14.4
Yes, 2+ biopsies	556	4.7	847	5.6	361	6.2	1764	5.4
Fracture at age 55+[d]								
No	11,484	97.2	12,898	85.4	4466	76.3	28,848	88.0
Yes	325	2.8	2203	14.6	1391	23.7	3919	12.0
Number of falls in last 12 mo								
None	8057	66.2	10,352	67.3	3984	66.8	22,393	66.8
1	2471	20.3	3094	20.1	1242	20.8	6807	20.3
2	1044	8.6	1322	8.6	522	8.7	2888	8.6
3+	594	4.9	619	4.0	220	3.7	1433	4.3

PHT, postmenopausal hormone therapy; E-alone, estrogen alone; E + P, estrogen + progestin.
[a]Hysterectomy at randomization.
[b]Applies only to participants who have ever been pregnant.
[c]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.
[d]Applies only to participants age 55 and older.

five women reporting exercise at least 4 times per week. More than half of women (57.9%) reported some weekly alcohol consumption (Table 1).

Current use of postmenopausal hormones (personal hormone use independent of the PHT component) was most common among women in their fifties (43.8%). In addition, one-third of women in their sixties used hormones (33.8%) and one in five women in their seventies were taking their own hormones at baseline (21.6%). The total duration of hormone use exceeded 10 years in 17.3% of women. At entry into the CaD trial, 30.5% of women reported use of their own hormones (data not shown). At randomization in the CaD trial, an additional 44.5% of the CaD cohort received hormone study medication (either active or placebo). The prevalence of other medications for the treatment of osteoporosis in this cohort was low at two to three percent (data not shown).

Personal history of fracture after age 55 was strongly associated with age: 2.8% of women aged 55 to 59 years, 14.6% of women aged 60 to 69 years and 23.7% of women aged 70 years and older reported having a prior fracture. Two-thirds of women reported no falls in the year prior to baseline, whereas 12.9% reported two or more falls. Parental history of fracture after age 40 was reported by 40.4% of women. One in six women reported a family history of colon cancer (16.2%).

TABLE 3. Dietary intake of WHI Calcium and Vitamin D participants by age, from a Food Frequency Questionnaire[1]

	Age at screening (y)							
	50–59 (N = 13,422)		60–69 (N = 16,520)		70–79 (N = 6340)		Total (N = 36,282)	
Nutrient[a]	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
Energy (kcal)	13,170	1670 ± 655	16,208	1607 ± 610	6205	1526 ± 574	35,583	1616 ± 622
Total fat (g)	13,170	68 ± 32	16,208	65 ± 30	6205	60 ± 28	35,583	65 ± 31
Total carbohydrate (g)	13,170	189 ± 77	16,208	182 ± 72	6205	179 ± 69	35,583	184 ± 73
Protein (g)	13,170	68 ± 28	16,208	66 ± 27	6205	62 ± 25	35,583	66 ± 27
Total SFA (g)	13,170	23 ± 12	16,208	22 ± 11	6205	20 ± 10	35,583	22 ± 11
Total trans fatty acid (g)	13,170	4.2 ± 1.9	16,208	4.0 ± 1.8	6205	3.7 ± 1.7	35,583	4.0 ± 1.8
Dietary fiber (g)	13,170	15 ± 6	16,208	15 ± 6	6205	15 ± 6	35,583	15 ± 6
Cholesterol (mg)	13,170	223 ± 119	16,208	214 ± 112	6205	195 ± 105	35,583	214 ± 114
Total alpha-toc eq (mg)	13,170	8.4 ± 3.4	16,208	8.4 ± 3.4	6205	8.2 ± 3.3	35,583	8.3 ± 3.4
Vitamin C (mg)	13,170	82 ± 46	16,208	88 ± 48	6205	96 ± 50	35,583	87 ± 48
Folacin (mcg)	13,170	216 ± 91	16,208	226 ± 92	6205	231 ± 93	35,583	223 ± 92
Calcium (mg)	13,170	681 ± 362	16,208	678 ± 354	6205	671 ± 356	35,583	678 ± 357
Fruits and vegetables (servings/day)	13,170	3.1 ± 1.3	16,208	3.4 ± 1.4	6205	3.8 ± 1.5	35,583	3.4 ± 1.4

[a]Means and standard deviations were computed on the log scale and back-transformed values are reported.

Calcium Intake and Other Dietary Characteristics (Tables 1 and 3; Figures 1 and 2)

The average baseline dietary calcium consumption among CaD trial participants was 678 mg/day. One-fourth of the women (23.9%) reported taking their own calcium supplements at baseline with the highest prevalence of use among women in their seventies (27.4%). These results were similar at randomization into CaD (data not shown). Based upon the combination of diet and supplement use, about one in ten women (9.1%: *n = 3,248 of 35,583 women with measured total calcium*) had a total calcium intake that was below 400 mg/day (Figure 1). One-third of women (35.1%) had a total calcium intake of at least 1200 mg/day, which is the Dietary Reference Intake for calcium (22). White women were more likely to consume at least 1200 mg/day (37.7%) than women in other race/ethnicity groups, whereas Black women were the least likely to consume this amount (16.9%) (Figure 1). Two-thirds of Black women (64.2%) reported total calcium consumption of ≤800 mg/day. Total intake of calcium varied little by age (Figure 2). Women consumed, on average, about 15 grams of fiber per day (Table 3).

Prevalence of Osteoporosis by Ethnicity and Age (Figures 3 and 4; Table 4)

Figure 3 shows the percentage of women in the bone density cohort classified as normal, osteopenic or osteoporotic as determined by the total hip BMD based on World Health Organization (WHO) BMD cutpoints (24). The reference group for defining these cutpoints was non-Hispanic White women aged 20 to 29 years in the Third National Health and Nutrition Examination Survey, 1988-94 (1). The prevalence of osteoporosis (>2.5 standard deviations below the mean of young adult White women) was low among

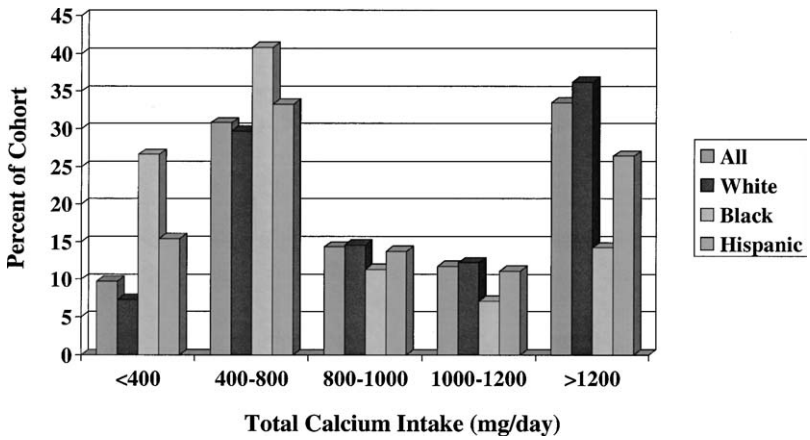

FIGURE 1. Total calcium intake of CaD participants by ethnicity.

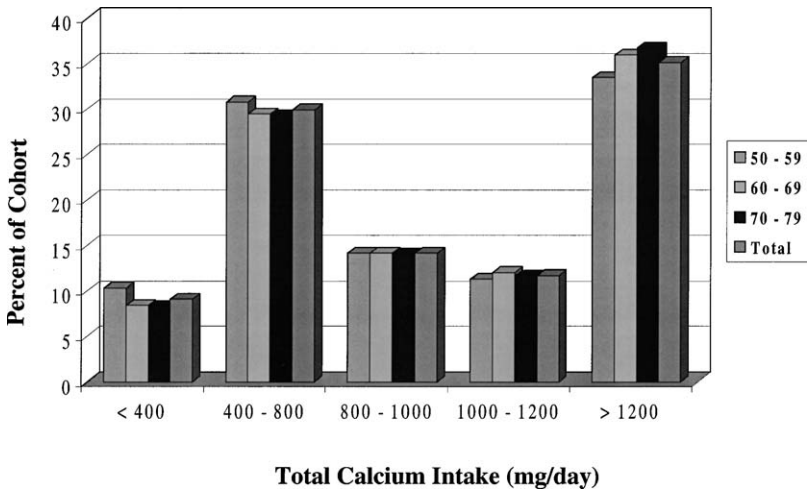

FIGURE 2. Total calcium intake of CaD participants by age.

WHI CaD trial participants: 4.5% of White women, 0.35% of Black women, and 2.7% of Hispanic women (Figure 3). About 39% of White and Hispanic women were classified with osteopenia (total hip BMD 1–2.5 standard deviations below the mean of young White women) compared with 32% of Black women. As expected, the prevalence of osteoporosis and osteopenia was strongly associated with older age (Figure 4 and Table 4). Among women in their seventies, 53.6% were classified with osteopenia and 9.3% with osteoporosis.

DISCUSSION

The WHI CaD Trial is the largest randomized, placebo-controlled clinical trial with the longest duration of exposure and follow-up testing the impact of calcium plus vitamin D supplementation on the incidence of hip and all fractures. There have been many published randomized clinical trials testing the effects of calcium supplementation on changes in BMD (4–9), an intermediate variable for treatment efficacy for osteoporosis. However, few randomized clinical trials have explored the role of calcium and vitamin D in the prevention of osteoporotic fracture (10–15). These few randomized clinical trials of fracture reduction are limited by small sample sizes, short duration of follow-up (less than 4.5 years), and few fractures in each trial. The WHI CaD trial should substantially contribute to the knowledge base on the impact of CaD on fractures. This cohort differs significantly from all of these published trials by reflecting a broader age distribution and ethnic diversity. The anticipated frequency of all fractures, and specifically hip fractures, across the duration of the study is sufficiently high to allow for potential analyses by age and/or ethnicity.

Based on current data, it has been postulated that CaD supplementation may be more effective in reducing fractures among patients with low calcium intake. These data are potentially consistent with the theory of calcium as a

TABLE 4. Baseline bone mineral density from a sample of WHI Calcium and Vitamin D participants by age

	Age at screening (y)											
	50–59 (N = 962)			60–69 (N = 1086)			70–79 (N = 481)			Total (N = 2529)		
BMD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD
Total hip BMD (WHO criteria)												
Normal	671	71.2		593	55.4		176	37.1		1440	57.9	
Osteopenic	261	27.7		434	40.6		254	53.6		949	38.2	
Osteoporotic	10	1.1		43	4.0		44	9.3		97	3.9	
Hip scan (g/cm^2)	962		0.9 ± 0.13	1085		0.9 ± 0.13	479		0.8 ± 0.12	2526		0.9 ± 0.14
Spine scan (g/cm^2)	952		1.0 ± 0.15	1065		1.0 ± 0.16	453		1.0 ± 0.17	2470		1.0 ± 0.16
Whole body scan (g/cm^2)	962		1.1 ± 0.10	1086		1.0 ± 0.10	481		1.0 ± 0.11	2529		1.0 ± 0.11
Lean body mass + BMC (kg)	950		41.4 ± 5.6	1072		40.3 ± 5.5	475		38.2 ± 5.0	2497		40.3 ± 5.6
Fat body mass (kg)	950		35.0 ± 11.6	1072		34.2 ± 10.7	475		31.4 ± 10.2	2497		34.0 ± 11.0

BMD, bone mineral density; WHO, World Health Organization; BMC, bone mineral content.

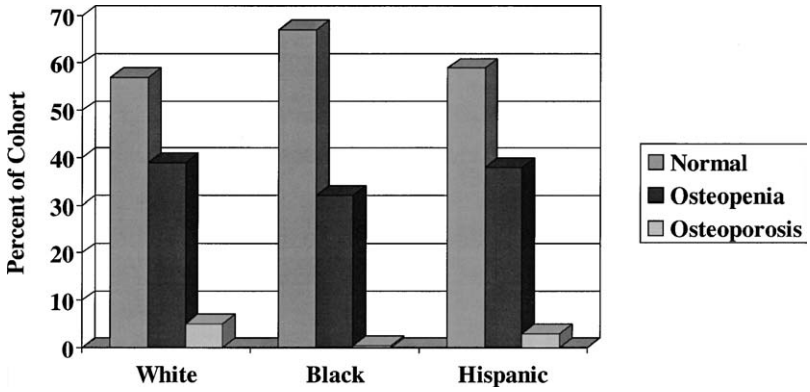

FIGURE 3. Prevalence of osteoporosis at the total hip among CaD participants by ethnicity.

"threshold" nutrient that affects bone density up to certain level beyond which further increases are of decreasing benefit (25). The WHI CaD trial, by way of the protocol that permits women to continue to use their own calcium and vitamin D supplements, offers a unique opportunity to explore this relationship further. Through both dietary and supplemental sources of calcium, self-selected total calcium intakes in the WHI CaD cohort ranges from less than 400 mg of elemental calcium per day to more than 1200 mg per day. In the group randomized to active CaD, the upper range will expand to a maximum of 2200 mg of calcium per day. This wide range of total calcium intakes will facilitate the first large-scale scrutiny of the optimal calcium intake for fracture prevention.

Women enrolled in the WHI CaD trial differ from their age-similar peers in the US population in several ways. About 41% of WHI CaD women had a college degree or higher education compared with 16% of women aged 50 to 79 years in the Third National Health and Nutrition Examination Survey, 1988-1994 (NHANES III), a nationally representative sample of women in the United States (1, 26). WHI CaD women are less likely to be current smokers than NHANES III women (e.g., 10.4% vs. 22.9% current smokers aged 50 to 59 years, respectively). Conversely, nearly 40% of WHI CaD women consume alcoholic beverages at least weekly compared with about 20% of NHANES III women. WHI CaD women are somewhat heavier than women in NHANES III. Their average body mass index ranged from 28.2 to 29.3 kg/M^2 compared with a range of 26.4 to 28.0 kg/M^2 among NHANES III women in comparable age groups. Dietary calcium intake (not including supplements) was about 130 mg/day higher on average among WHI CaD women as compared with NHANES III women (approximately 678 mg/day vs. 547 mg/day, respectively). These differences are consistent with a healthy volunteer effect.

The percentage of women in the bone density cohort classified as having osteoporosis using the WHO definition is also considerably lower in the WHI CaD trial than in NHANES III. This is true for both White and Black women. In contrast, the percentages of women in the WHI CaD trial who met WHO criteria for osteopenia were similar to those reported from NHANES III. The lower prevalence of osteoporosis in the CaD cohort may reflect their personal use of hormones, higher degree of obesity, higher total

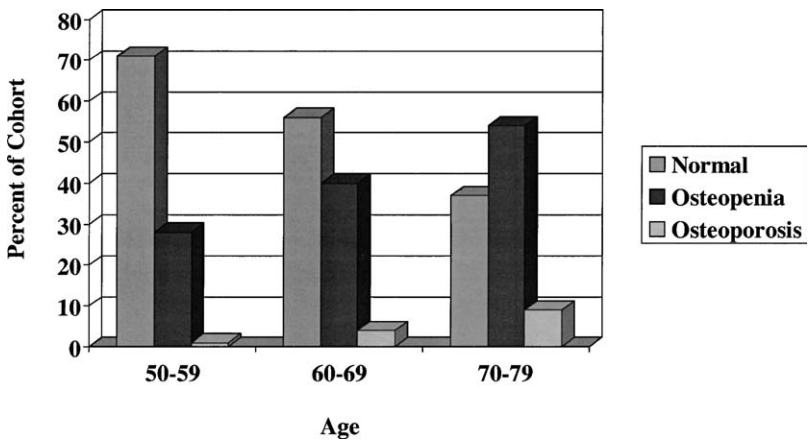

FIGURE 4. Prevalence of osteoporosis at the total hip among CaD participants by age.

calcium intake or lower levels of other osteoporosis risk factors.

Both the observational data for vitamin D and the limited clinical trial data on calcium support promising opportunities for colon cancer prevention. A recent randomized controlled trial of the effect of calcium supplementation (1200 mg) on recurrence of colorectal adenomas in 930 subjects reported about a 15% reduction in the risk of recurrent adenomas (16). Seventy-two percent of the participants in that trial were male and results were not presented for men and women separately. The WHI CaD trial will extend these observations by contributing information on the effect of a wide range of calcium intakes on colorectal cancer in a lower risk population of women. Vitamin D intake has been associated with reduction in colon cancer risk in several observational studies (17–20). In the Nurses Health Study, colon cancer was only one third as high in women who consistently consumed vitamin D (21). The combination in the CaD trial will be the first large-scale test of the calcium/vitamin D hypothesis for colon cancer prevention in women and it will provide unbiased estimates of effects on a range of other clinical events.

In summary, the WHI CaD trial will provide rigorous tests of the hypotheses that CaD supplementation reduces risk of fracture and colorectal cancer in post-menopausal women. This trial has the largest sample size, longest duration of follow-up, and widest distribution of calcium intake of any clinical trial to date. These strengths will also permit evaluation of treatment effect in important sub-groups of women, including those of different ages, different race and ethnic backgrounds and at different levels of baseline risk.

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ELSEVIER

The Women's Health Initiative Observational Study: Baseline Characteristics of Participants and Reliability of Baseline Measures

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INTRODUCTION

The Women's Health Initiative (WHI) Observational Study (OS) was established to explore the predictors and natural history of important causes of morbidity and mortality in postmenopausal women, and to serve as a secular control for the WHI Clinical Trial (CT). It enrolled 93,676 ethnically diverse women born in four different decades, from those who came of age in the depression-era, to the first members of the baby boom. Accordingly, this cohort reflects a wide range of socio-cultural influences on opportunities and health behaviors.

OS participants will contribute longitudinal data on health status, risk exposures and disease events. The follow-up interval will be slightly shorter than that in the clinical trial, approximately 7 years. All OS women had a physical examination at baseline and 3 years. Additional data are obtained with annual mailed questionnaires. These forms explore risk exposures, health behaviors, and the prevalence of less common diseases to provide a comprehensive view of both classical and novel risk factors, as well as secular trends in the predictors of healthy aging and disease events. Because of its size, the OS will permit exploration of factors associated with less common diseases.

This article describes the demographic, reproductive, dietary, and health characteristics of the OS women by ethnicity and age. In addition, we present information on the reliability of many of the baseline measures assessed in a subset of participants who were selected for the Measurement Precision Study (OS-MPS).

METHODS

Study participants were enrolled at 40 centers throughout the United States between October 1, 1993 and December 31, 1998. Potential subjects were excluded if they did not plan to reside in the area for at least 3 years, had medical conditions predictive of survival less than 3 years, or had complicating conditions such as alcoholism, drug dependency or dementia. All participants provided informed consent using materials approved by institutional review boards at each center. Details of the scientific rationale, eligibility requirements and other aspects of the design of the WHI have been published (1).

Participants entered the OS by expressing interest in either the diet modification (DM) or postmenopausal hormone therapy (PHT) components of the clinical trial, but proving ineligible or unwilling to participate in the clinical trial, or by responding to a direct invitation to be screened for the OS. Thus, the specific exclusions for the DM and PHT components influenced the characteristics of women in the OS. Those exclusions are outlined in Hays' article in this issue.

Data Collection and Definition of Variables

Demographic and risk exposure data, as well as data regarding family and medical history, were obtained by self-report using standardized questionnaires. Certified staff took physical measurements, including blood pressure, height and weight, and blood samples at the clinic visit. Most blood is reserved for nested case-control studies, but levels of certain nutrients and cardiovascular risk markers, assayed in a subsample, are reported here. A standardized written protocol, centralized training of local clinic staff, local quality assurance activities, and periodic quality assurance visits by the

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Clinical Coordinating Center were used to maintain uniform data collection procedures at all study sites. Additional details can be found in the appendix to Anderson's article.

Statistical Analyses

Distributions of categorical variables were calculated in strata defined by age and ethnicity, and the chi-square statistic was used to assess group differences. For continuous variables, means and standard deviations were calculated for these same strata, and analysis of variance (ANOVA) was used to assess the significance of differences between age and ethnic categories, with and without adjustment for effect modifiers.

Since the sample size was very large, tests for statistical significance were highly significant ($p < 0.001$) for nearly all comparisons. Accordingly, the level of statistical significance is not shown in the tables. Age-adjustment was applied to all variables but only meaningfully affected the fractions living alone, widowed, and with hysterectomy. Given the limited utility of age-adjustment with so few factors affected, unadjusted rates are reported in all tables. All contrasts noted in the results were statistically significant with or without adjustment; the items highlighted were chosen based on either the magnitude of differences or "ad hoc" hypotheses.

Reliability Subsample

The test-retest reliability of selected measures was assessed in a subset of OS women who participated in the Measurement Precision Study. The self-administered baseline questionnaires and the blood draw were repeated approximately 3 months after baseline. Physical measures and interviewer-administered questionnaires were not included. The Food Frequency Questionnaire (FFQ) was not repeated because it was assessed in a separate study (2).

A predefined number of women who enrolled in the OS between October 1996 and June 1997 were randomly selected each month and invited to join the OS-MPS at the time of their entry into the WHI. Sampling was stratified by center, age, and race/ethnicity and continued until 1000 women agreed to participate. To reduce burden, each participant repeated four of the original eight questionnaires based on a random assignment of clinics into two groups. Thus, the reliability of each variable was tested in approximately half of the women participating in the OS-MPS.

Overall, 2045 women were selected, 1092 completed the repeat questionnaires, and 872 had the repeat fasting blood draw. The average time between measures was 3 months (range: 8–15 weeks). The response rate was greater than the apparent 53% because some women who enrolled did not participate 3 months later as their clinic had reached its quota.

Kappa statistics were calculated for dichotomous or nominal categorical variables, weighted kappa was used for ordered categorical variables, and the intra-class correlation coefficient (ICC) was used for continuous measures (the blood measures) (3). The distributions of the blood analytes were generally positively skewed; however, the ICCs with and without log transformation were almost identical, so the untransformed values are given. These statistics are reported in Tables 1, 2, and 4 alongside the primary study data for the items assessed.

RESULTS

93,726 women enrolled in the OS between September 1, 1994 and December 31, 1998. Of these, 31 provided insufficient baseline data to be included in these analyses, and 19 duplicate enrollments were found across multiple sites. After removing these, the remaining 93,676 women form the final analytic OS cohort, of which 78,013 (83.3%) were White, 7,639 (8.2%) Black, 3,623 (3.9%) Hispanic, 2,671 (2.9%) Asian/Pacific Islander, 422 (0.57%) American Indian, and 1308 (1.4%) of unknown race/ethnicity. The age distribution was 31.7%, 44.0% and 24.3%, respectively, for groups 50 to 59, 60 to 69, and 70 to 79 years old. Comparisons between OS and CT participants can be made by contrasting the tables presented in similar formats in this and preceding articles as well as in the appendix to Hays' article.

Age Contrasts

Educational attainment, occupational level, and total family income declined with age (Table 1). Twenty-five percent of the women aged 70 to 79 years had total family income less than $20,000 compared with 10% of women aged 50 to 59 years. Conversely, over half the women aged 50 to 59 years reported family incomes greater than $50,000 compared with about 25% of women aged 70 to 79 years.

Current smoking was inversely associated with age, declining by 2% for each decade from a maximum of 8% in women 50 to 59 years old. Women 70 to 79 years old were the least likely to have ever smoked. Current alcohol use decreased with age, and older women were more likely to be past drinkers. The frequency of moderate or greater physical activity decreased with age. Conversely, the youngest age group reported more hours sedentary. Body Mass Index (BMI) was lowest in women 70 to 79 years old, but waist/hip ratio increased slightly with age.

All participants were postmenopausal so childbearing was complete. Nonetheless, women in the oldest two age groups reported more pregnancies and live births than women aged 50 to 59 years (Table 2). Yet, a greater

TABLE 1. Baseline demographic and general health characteristics of WHI Observational Study participants by age

	Age at screening (y)												
	50–59 (N = 29,705)			60–69 (N = 41,197)			70–79 (N = 22,774)			Total (N = 93,676)			Reliability (N = 564)
Characteristic	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	κ
Race/Ethnicity													0.99
American Indian	178	0.6		161	0.4		83	0.4		422	0.5		
Asian/Pacific Islander	861	2.9		1102	2.7		708	3.1		2671	2.9		
Black	2978	10.0		3256	7.9		1405	6.2		7639	8.2		
Hispanic	1761	5.9		1399	3.4		463	2.0		3623	3.9		
White	23,565	79.3		34,677	84.2		19,771	86.8		78,013	83.3		
Unknown	362	1.2		602	1.5		344	1.5		1308	1.4		
Education													0.87[a]
0–8 years	433	1.5		612	1.5		515	2.3		1560	1.7		
Some high school	676	2.3		1572	3.8		1040	4.6		3288	3.5		
High school diploma/GED	3715	12.6		7343	18.0		4063	18.0		15,121	16.3		
School after high school	10,422	35.4		14,793	36.2		8718	38.6		33,933	36.5		
College degree or higher	14,173	48.2		16,560	40.5		8269	36.6		39,002	42.0		
Family income													0.81[a]
<$10,000	991	3.5		1648	4.3		1277	6.2		3916	4.5		
$10,000–$19,999	1744	6.2		4460	11.7		3896	18.8		10,100	11.6		
$20,000–$34,999	4266	15.2		9640	25.3		6320	30.5		20,226	23.3		
$35,000–$49,999	5143	18.4		8167	21.5		4119	19.9		17,429	20.1		
$50,000–$74,999	6951	24.8		7551	19.8		2984	14.4		17,486	20.2		
$75,000 +	8880	31.7		6603	17.3		2125	10.3		17,608	20.3		
Occupation													0.64
Managerial/Professional	13,945	49.1		16,540	42.1		8137	37.8		38,622	43.3		
Technical/Sales/Administrative	7951	28.0		11,512	29.3		6017	28.0		25,480	28.6		
Service/Labor	4537	16.0		6813	17.3		4120	19.2		15,470	17.3		
Homemaker only	1964	6.9		4457	11.3		3237	15.0		9658	10.8		
Body mass index (BMI), kg/m^2	29,353		27.5 ± 6.3	40,696		27.4 ± 5.8	22,519		26.7 ± 5.3	92,568		27.3 ± 5.9	
Height (cm)	29,491		163.1 ± 6.8	40,846		161.7 ± 6.6	22,583		159.7 ± 6.5	92,920		161.7 ± 6.8	
Weight (kg)	29,536		73.4 ± 18.0	40,988		72.2 ± 16.7	22,680		68.6 ± 15.1	93,204		71.7 ± 16.9	
Waist/hip ratio (WHR)	29,555		0.8 ± 0.1	40,960		0.8 ± 0.1	22,652		0.8 ± 0.1	93,167		0.8 ± 0.1	
Waist (cm)	29,588		84.2 ± 14.4	41,017		85.4 ± 13.7	22,674		84.6 ± 12.5	93,279		84.8 ± 13.7	
Marital status													0.95
Never married	1618	5.5		1764	4.3		1008	4.5		4390	4.7		
Divorced/Separated	6048	20.5		6234	15.2		2445	10.8		14,727	15.8		
Widowed	1676	5.7		6795	16.6		7819	34.5		16,290	17.5		
Presently married/Living as married	20,218	68.4		26,212	63.9		11,375	50.2		57,805	62.0		
Living alone													0.89
No	24,010	81.4		30,463	74.5		13,837	61.3		68,310	73.5		
Yes	5476	18.6		10,409	25.5		8718	38.7		24,603	26.5		
U.S. region													
Northeast	6309	21.2		10,007	24.3		4957	21.8		21,273	22.7		
South	8919	30.0		10,380	25.2		5163	22.7		24,459	26.1		
Midwest	6457	21.7		9436	22.9		4714	20.7		20,607	22.0		
West	8023	27.0		11,374	27.6		7940	34.9		27,337	29.2		

(*continued*)

TABLE 1. *Continued*

Characteristic	Age at screening (y) 50–59 (N = 29,705) N	%	Mean ± SD	60–69 (N = 41,197) N	%	Mean ± SD	70–79 (N = 22,774) N	%	Mean ± SD	Total (N = 93,676) N	%	Mean ± SD	Reliability (N = 564) κ
Years lived in current state													0.73[a]
<5	1297	4.4		1439	3.5		586	2.6		3322	3.6		
5–9	1447	4.9		1401	3.4		736	3.3		3584	3.9		
10–19	3298	11.2		2749	6.7		1393	6.2		7440	8.0		
20+	23,468	79.5		35,330	86.3		19,882	88.0		78,680	84.6		
Born in the U.S.													1.00
No	2422	8.2		2876	7.0		1504	6.6		6802	7.3		
Yes	27,098	91.8		38,053	93.0		21,130	93.4		86,281	92.7		
U.S. region of birth													0.99
Not born in U.S.	2422	8.3		2876	7.1		1504	6.7		6802	7.4		
Northeast	7769	26.5		11,807	29.0		6187	27.5		25,763	27.9		
Midwest	7970	27.2		12,144	29.9		6963	30.9		27,077	29.3		
South	7156	24.4		8683	21.3		4479	19.9		20,318	22.0		
West	3972	13.6		5160	12.7		3366	15.0		12,498	13.5		
Smoking													0.94
Never smoked	14,427	49.1		20,246	49.8		12,350	55.4		47,023	50.9		
Past smoker	12,570	42.8		17,884	44.0		9060	40.6		39,514	42.8		
Current smoker	2386	8.1		2503	6.2		902	4.0		5791	6.3		
Years as a child lived with smoker													0.83[a]
Never lived with a smoker	8375	28.7		14,528	36.1		10,234	46.4		33,137	36.2		
<1	269	0.9		350	0.9		200	0.9		819	0.9		
1–4	895	3.1		1138	2.8		569	2.6		2602	2.8		
5–9	1891	6.5		2241	5.6		1114	5.0		5246	5.7		
10–18	17,704	60.8		21,979	54.6		9953	45.1		49,636	54.3		
Years as adult lived with smoker													0.73[a]
Never lived with a smoker	8573	29.2		10,114	24.8		5675	25.3		24,362	26.3		
<1	793	2.7		775	1.9		444	2.0		2012	2.2		
1–4	3801	12.9		3707	9.1		1647	7.3		9155	9.9		
5–9	3404	11.6		3550	8.7		1619	7.2		8573	9.3		
10–19	5145	17.5		6588	16.2		2917	13.0		14,650	15.8		
20–29	3868	13.2		6526	16.0		3494	15.6		13,888	15.0		
30–39	2804	9.5		4949	12.2		3015	13.4		10,768	11.6		
40+	1015	3.5		4498	11.0		3620	16.1		9133	9.9		
Years worked with smoker													0.63[a]
Never worked with a smoker	7040	24.0		10,034	24.7		6269	27.9		23,343	25.3		
<1	1223	4.2		1396	3.4		758	3.4		3377	3.7		
1–4	5509	18.8		6039	14.9		2969	13.2		14,517	15.7		
5–9	5314	18.1		6134	15.1		2856	12.7		14,304	15.5		
10–19	5653	19.3		7870	19.4		3885	17.3		17,408	18.8		
20–29	3241	11.0		5403	13.3		3078	13.7		11,722	12.7		
30–39	1129	3.8		2555	6.3		1557	6.9		5241	5.7		
40+	243	0.8		1225	3.0		1058	4.7		2526	2.7		

Alcohol intake									
Never drinker	2736	9.3	4566	11.2	3175	14.1	10,477	11.3	
Past drinker	5303	17.9	7534	18.4	4718	20.9	17,555	18.9	
<1 drink per mo	3869	13.1	4567	11.2	2297	10.2	10,733	11.5	
<1 drink per wk	6143	20.8	8216	20.1	4369	19.4	18,728	20.1	
1–<7 drinks per wk	8059	27.3	10,541	25.8	5242	23.2	23,842	25.6	
7 + drinks per wk	3448	11.7	5487	13.4	2774	12.3	11,709	12.6	
Physical activity									0.67[a]
No activity	4213	14.3	5343	13.1	3081	13.7	12,637	13.6	
Some activity	10,432	35.5	15,560	38.2	9656	42.9	35,648	38.5	
2–<4 episodes per wk of moderate + activity	5304	18.1	7686	18.9	4103	18.2	17,093	18.5	
4 + episodes per wk of moderate + activity	9425	32.1	12,144	29.8	5682	25.2	27,251	29.4	
Total expenditure/wk from physical activity (METs)									0.77[a]
0–1.5	5904	2.01	7602	18.7	4382	19.5	17,888	19.3	
>1.5–8	7215	24.6	10,089	24.8	6026	26.8	23,330	25.2	
>8–19	8400	28.6	12,119	29.8	6686	29.7	27,205	29.4	
>19	7855	26.7	10,923	26.8	5428	24.1	24,206	26.1	
Hours/day spent sitting, sleeping or lying down									0.60[a]
4–12.5	6364	21.7	9569	23.5	5586	24.9	21,519	23.2	
13–14.5	4408	15.0	7564	18.6	4355	19.4	16,327	17.6	
15–16.5	4837	16.5	7955	19.5	4608	20.5	17,400	18.8	
17+	13,776	46.9	15,686	38.5	7926	35.3	37,388	40.4	
Any supplement use									
No	9287	31.3	10,745	26.1	5535	24.3	25,567	27.3	
Yes	20,418	68.7	30,452	73.9	17,239	75.7	68,109	72.7	
Multivitamin use (with or without minerals)									
No	18,261	61.5	23,682	57.5	12,897	56.6	54,840	58.5	
Yes	11,444	38.5	17,515	42.5	9877	43.4	38,836	41.5	
Vitamin C as single supplement									
No	21,975	74.0	28,825	70.0	15,794	69.4	66,594	71.1	
Yes	7730	26.0	12,372	30.0	6980	30.6	27,082	28.9	
Vitamin E as single supplement									
No	20,859	70.2	26,835	65.1	14,638	64.3	62,332	66.5	
Yes	8846	29.8	14,362	34.9	8136	35.7	31,344	33.5	
Calcium as single supp (including antacids)									
No	21,894	73.7	29,194	70.9	15,902	69.8	66,990	71.5	
Yes	7811	26.3	12,003	29.1	6872	30.2	26,686	28.5	
Single supplement (not vitamin C, E, or calcium)									
No	17,926	60.3	23,709	57.6	13,063	57.4	54,898	58.4	
Yes	11,779	39.7	17,488	42.4	9711	42.6	38,978	41.6	

[a]Weighted kappa.

Table 2. Baseline reproductive and medical history status of WHI Observational Study participants by age

	Age at screening (y)												
	50–59 (N = 29,705)			60–69 (N = 41,197)			70–79 (N = 22,774)			Total (N = 93,676)			Reliability (N = 564)
Reproductive and Medical History	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	N	%	Mean ± SD	κ
Hysterectomy[b]													0.95
No	18,047	60.8		23,694	57.6		12,702	55.8		54,443	58.2		
Yes	11,628	39.2		17,463	42.4		10,056	44.2		39,147	41.8		
Age at hysterectomy (y)													0.92[a]
Not hysterectomized	18,047	60.9		23,694	57.7		12,702	55.9		54,443	58.3		
<40	4918	16.6		5367	13.1		2174	9.6		12,459	13.3		
40–49	5090	17.2		7677	18.7		4025	17.7		16,792	18.0		
50–54	1297	4.4		2167	5.3		1635	7.2		5099	5.5		
55+	285	1.0		2191	5.3		2175	9.6		4651	5.0		
Ever pregnant													0.98
No	3272	11.0		3660	8.9		2425	10.7		9357	10.0		
Yes	26,348	89.0		37,404	91.1		20,252	89.3		84,004	90.0		
Age at first birth (y)[c]													0.86[a]
Never had term pregnancy	1134	4.7		859	2.6		544	3.1		2537	3.4		
<20	4301	17.9		4758	14.3		1458	8.4		10,517	14.1		
20–29	16,664	69.2		24,962	74.9		12,887	74.2		54,513	72.9		
30+	1969	8.2		2763	8.3		2473	14.2		7205	9.6		
Number of pregnancies													0.97[a]
Never pregnant	3272	11.1		3660	8.9		2425	10.7		9357	10.0		
1	2632	8.9		2449	6.0		1699	7.5		6780	7.3		
2–4	18,845	63.7		23,844	58.2		13,090	57.9		55,779	59.9		
5+	4819	16.3		11,021	26.9		5411	23.9		21,251	22.8		
Number of live births													0.98[b]
Never pregnant	3272	11.1		3660	8.9		2425	10.7		9357	10.1		
None	1186	4.0		920	2.2		591	2.6		2697	2.9		
1	3405	11.5		3208	7.8		2166	9.6		8779	9.4		
2–4	19,581	66.4		26,776	65.5		14,317	63.4		60,674	65.2		
5+	2066	7.0		6340	15.5		3094	13.7		11,500	12.4		
Any induced abortions[c]													0.71
Pregnant, never had an abortion	21,658	86.5		32,289	92.9		17,520	94.0		71,467	91.1		
One or more abortions	3385	13.5		2464	7.1		1116	6.0		6965	8.9		
Number of months breastfed													0.89[a]
Never breastfed	15,316	52.1		19,949	49.2		10,178	45.8		45,443	49.3		
1–6	6892	23.4		10,707	26.4		6269	28.2		23,868	25.9		
7–12	3313	11.3		4322	10.7		2613	11.7		10,248	11.1		
13–23	2396	8.1		3448	8.5		1918	8.6		7762	8.4		
24+	1487	5.1		2152	5.3		1261	5.7		4900	5.3		
Age at tubal ligation (y)													0.94
Never had tubal ligation	20,509	69.5		35,522	86.9		21,259	94.3		77,290	83.2		
<30	1154	3.9		844	2.1		324	1.4		2322	2.5		
30–34	2964	10.0		1058	2.6		395	1.8		4417	4.8		
35–39	3298	11.2		1679	4.1		358	1.6		5335	5.7		
40–44	1343	4.6		1380	3.4		155	0.7		2878	3.1		
45+	246	0.8		404	1.0		54	0.2		704	0.8		

Age last had any menstrual bleeding (y)												0.83[a]
<40	4207	15.8		4725	12.4		1904	9.0		10,836	12.6	
40–44	3329	12.5		5448	14.3		2867	13.6		11,644	13.6	
45–49	6120	23.0		7724	20.3		4572	21.7		18,416	21.5	
50–54	10,080	37.9		12,384	32.5		7670	36.4		30,134	35.1	
55–59	2894	10.9		5137	13.5		2678	12.7		10,709	12.5	
60+				2668	7.0		1355	6.4		4023	4.7	
Current health care provider												0.59
No	2002	6.8		1994	4.9		798	3.5		4794	5.2	
Yes	27,414	93.2		38,812	95.1		21,731	96.5		87,957	94.8	
Mammogram in last 2 y												
No	3936	13.6		5217	13.0		3557	16.2		12,710	14.0	
Yes	24,979	86.4		34,828	87.0		18,355	83.8		78,162	86.0	
Pap smear in last 3 y												
No	1109	6.6		1857	8.5		1624	14.2		4590	9.2	
Yes	15,625	93.4		19,982	91.5		9785	85.8		45,392	90.8	
History of PHT use[d]												
Never	9854	33.2		16,906	41.1		11,057	48.7		37,817	40.4	
Past	2965	10.0		5674	13.8		4493	19.8		13,132	14.0	
Current	16,846	56.8		18,565	45.1		7168	31.6		42,579	45.5	
Total PHT duration (y)												
Non-user	9854	33.2		16,906	41.0		11,057	48.6		37,817	40.4	
<5	10,071	33.9		6969	16.9		3791	16.6		20,831	22.2	
5–<10	5830	19.6		5262	12.8		1552	6.8		12,644	13.5	
10–<15	2482	8.4		5358	13.0		1447	6.4		9287	9.9	
15+	1467	4.9		6701	16.3		4927	21.6		13,095	14.0	
History of E-alone use[d]												
Never	19,266	64.9		25,635	62.3		13,443	59.2		58,344	62.4	
Past	2046	6.9		4735	11.5		4304	18.9		11,085	11.8	
Current	8356	28.2		10,787	26.2		4979	21.9		24,122	25.8	
Total E-alone duration (y)												
Non-user	19,266	64.9		25,635	62.2		13,443	59.0		58,344	62.3	
<5	4768	16.1		4798	11.6		3098	13.6		12,664	13.5	
5–<10	2948	9.9		2821	6.8		1220	5.4		6989	7.5	
10–<15	1511	5.1		2785	6.8		1050	4.6		5346	5.7	
15+	1212	4.1		5157	12.5		3963	17.4		10,332	11.0	
History of E+P use[d]												
Never	18,443	62.1		29,519	71.7		19,128	84.0		67,090	71.7	
Past	2544	8.6		3708	9.0		1380	6.1		7632	8.2	
Current	8705	29.3		7950	19.3		2252	9.9		18,907	20.2	
Total E+P duration (y)												
Non-user	18,443	62.1		29,519	71.7		19,128	84.0		67,090	71.6	
<5	7162	24.1		4628	11.2		1580	6.9		13,370	14.3	
5–<10	3098	10.4		3404	8.3		695	3.1		7197	7.7	
10–<15	842	2.8		2537	6.2		630	2.8		4009	4.3	
15+	159	0.5		1109	2.7		741	3.3		2009	2.1	
Systolic blood pressure (mm Hg)	29,665		120.7 ± 16.1	41,146		127.7 ± 17.4	22,740		133.8 ± 18.6	93,551		127.0 ± 18.0
≤120	16,191	54.6		15,290	37.2		5706	25.1		37,187	39.8	
>120–140	10,297	34.7		17,328	42.1		9764	42.9		37,389	40.0	
>140	3177	10.7		8528	20.7		7270	32.0		18,975	20.3	

(*continued*)

Table 2. *Continued*

Reproductive and Medical History	Age at screening (y) 50–59 (N = 29,705) N	%	Mean ± SD	60–69 (N = 41,197) N	%	Mean ± SD	70–79 (N = 22,774) N	%	Mean ± SD	Total (N = 93,676) N	%	Mean ± SD	Reliability (N = 564) κ
Diastolic blood pressure (mm Hg)	29,665		75.4 ± 9.2	41,137		75.0 ± 9.3	22,729		73.4 ± 9.6	93,531		74.7 ± 9.4	
<90	27,600	93.0		38,448	93.5		21,501	94.6		87,549	93.6		
≥90	2065	7.0		2689	6.5		1228	5.4		5982	6.4		
History of hypertension													0.86
Never hypertensive	22,029	75.3		26,195	64.8		12,975	58.1		61,199	66.5		
Untreated hypertensive	2192	7.5		3268	8.1		1858	8.3		7318	8.0		
Treated hypertensive	5035	17.2		10,948	27.1		7481	33.5		23,464	25.5		
Treated diabetes (pills or shots)													0.86
No	28,743	96.8		39,287	95.5		21,624	95.1		89,654	95.8		
Yes	938	3.2		1855	4.5		1109	4.9		3902	4.2		
Treated hypercholesterolemia (pills)													0.82
No	26,289	90.6		33,499	83.2		18,047	80.8		77,835	85.0		
Yes	2732	9.4		6761	16.8		4281	19.2		13,774	15.0		
Depression (shortened CES-D/DIS≥0.06)													0.49
No	24,836	85.5		35,950	89.6		19,972	91.0		80,758	88.6		
Yes	4204	14.5		4177	10.4		1987	9.0		10,368	11.4		
Benign breast disease													0.77
No	22,185	79.4		29,225	76.6		15,899	76.7		67,309	77.5		
Yes, 1 biopsy	4071	14.6		6100	16.0		3332	16.1		13,503	15.6		
Yes, 2+ biopsies	1673	6.0		2841	7.4		1487	7.2		6001	6.9		
History of MI													0.93
No	29,363	98.9		40,148	97.5		21,772	95.7		91,283	97.5		
Yes	319	1.1		1013	2.5		974	4.3		2306	2.5		
History of stroke													0.58
No	29,459	99.2		40,567	98.5		22,180	97.5		92,206	98.5		
Yes	235	0.8		602	1.5		578	2.5		1415	1.5		
History of CHF													0.44
No	29,559	99.5		40,792	99.0		22,427	98.5		92,778	99.0		
Yes	145	0.5		401	1.0		346	1.5		892	1.0		
History of angina													0.82
No	28,876	97.5		39,072	95.3		20,915	92.5		88,863	95.3		
Yes	729	2.5		1935	4.7		1708	7.5		4372	4.7		
History of carotid endarterectomy/angioplasty													0.67
No	29,333	99.9		40,406	99.7		22,087	99.2		91,826	99.6		
Yes	35	0.1		138	0.3		171	0.8		344	0.4		
History of DVT													0.58
No	28,844	97.2		39,450	95.8		21,727	95.5		90,021	96.2		
Yes	841	2.8		1710	4.2		1021	4.5		3572	3.8		
History of PE													0.89
No	29,473	99.3		40,708	98.9		22,479	98.8		92,660	99.0		
Yes	214	0.7		469	1.1		276	1.2		959	1.0		

History of peripheral arterial disease PAD									0.72
No	29,380	99.2	40,352	98.4	22,008	97.4	91,740	98.4	
Yes	231	0.8	643	1.6	593	2.6	1467	1.6	
History of CABG/PTCA									0.90
No	29,149	99.3	39,744	98.0	21,500	96.6	90,393	98.1	
Yes	217	0.7	799	2.0	757	3.4	1773	1.9	
History of polyp removal									0.88
No	27,252	94.1	35,693	89.4	18,781	85.6	81,726	90.0	
Yes	1709	5.9	4241	10.6	3160	14.4	9110	10.0	
History of fracture at age 55+[e]									0.65
No	16,176	94.8	34,368	84.8	16,882	75.4	67,426	84.3	
Yes	893	5.2	6148	15.2	5500	24.6	12,541	15.7	
History of hip fracture at age 55+									0.67
No	29,242	100.0	40,309	99.5	22,061	98.6	91,612	99.4	
Yes	10	0.0	207	0.5	321	1.4	538	0.6	
Number of falls in last 12 mo									0.45[a]
None	19,756	67.3	27,791	68.3	15,063	67.0	62,610	67.7	
1	5746	19.6	8063	19.8	4585	20.4	18,394	19.9	
2	2439	8.3	3219	7.9	1921	8.6	7579	8.2	
3+	1407	4.8	1607	4.0	897	4.0	3911	4.2	
History of cancer[f]									0.77
No	26,552	89.9	35,604	87.1	18,697	83.0	80,853	87.0	
Yes	2984	10.1	5270	12.9	3821	17.0	12,075	13.0	
History of breast cancer									0.89
No	28,436	95.8	38,925	94.6	21,171	93.1	88,532	94.6	
Yes	1233	4.2	2222	5.4	1566	6.9	5021	5.4	
History of colorectal cancer									1.00
No	29,504	99.6	40,733	99.1	22,325	98.3	92,562	99.1	
Yes	107	0.4	367	0.9	386	1.7	860	0.9	
History of endometrial cancer									0.82
No	29,260	98.6	40,450	98.3	22,120	97.3	91,830	98.2	
Yes	409	1.4	699	1.7	613	2.7	1721	1.8	
History of melanoma									0.76
No	29,258	98.8	40,332	98.2	22,116	97.5	91,706	98.2	
Yes	363	1.2	729	1.8	567	2.5	1659	1.8	
History of cervical cancer									1.00
No	29,071	98.6	40,310	98.7	22,178	98.8	91,559	98.7	
Yes	418	1.4	514	1.3	273	1.2	1205	1.3	
History of osteoporosis									0.77
No	27,973	95.5	36,860	90.7	19,325	85.8	84,158	91.0	
Yes	1325	4.5	3770	9.3	3187	14.2	8282	9.0	
History of arthritis									0.81
No arthritis	18,670	63.6	20,011	49.4	9006	40.5	47,687	51.8	
Rheumatoid arthritis	1253	4.3	2243	5.5	1479	6.6	4975	5.4	
Other arthritis	9425	32.1	18,221	45.0	11,767	52.9	39,413	42.8	

(*continued*)

Table 2. *Continued*

Reproductive and Medical History	Age at screening (y) 50–59 (N = 29,705) N	%	Mean ± SD	60–69 (N = 41,197) N	%	Mean ± SD	70–79 (N = 22,774) N	%	Mean ± SD	Total (N = 93,676) N	%	Mean ± SD	Reliability (N = 564) κ
Family history of myocardial infarction													0.83
No	14,655	51.7		17,863	45.7		9570	45.0		42,088	47.5		
Yes	13,698	48.3		21,196	54.3		11,675	55.0		46,569	52.5		
Family history of stroke													0.84
No	18,905	66.9		23,218	59.9		12,278	57.5		54,401	61.6		
Yes	9333	33.1		15,565	40.1		9061	42.5		33,959	38.4		
Family history of breast cancer													0.92
No	23,088	81.8		31,306	80.4		16,948	79.5		71,342	80.6		
Yes	5148	18.2		7622	19.6		4360	20.5		17,130	19.4		
Family history of colorectal caner													0.85
No	23,564	86.2		31,195	82.8		16,402	80.1		71,161	83.2		
Yes	3782	13.8		6458	17.2		4079	19.9		14,319	16.8		
Parent broke bone after age 40													0.88
No	16,480	59.9		22,545	59.2		13,148	62.8		52,173	60.3		
Yes	11,031	40.1		15,516	40.8		7793	37.2		34,340	39.7		
Family history of adult diabetes													0.88
No	18,954	66.8		25,848	66.1		14,671	68.6		59,473	66.9		
Yes	9416	33.2		13,262	33.9		6725	31.4		29,403	33.1		

MI, myocardial infarction; CHF, congestive heart failure; DVT, deep vein thrombosis; PE, pulmonaryembolism.
[a]Weighted kappa.
[b]Hysterectomy at randomization.
[c]Applies only to participants who have ever been pregnant.
[d]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.
[e]Applies only to participants age 55 and older.
[f]Excluding non-melanoma skin cancer.

fraction of women 70 to 79 years old had their first child after age 30 than women in the younger age cohorts.

The prevalence of diabetes, hypertension, prior myocardial infarction, stroke, cancer, fracture, and hysterectomy increased with age. Access to a health care provider increased, but the frequency of mammography and Pap smears declined with age. Women 50 to 59 years old were the most likely to be depressed, with a prevalence about 50% greater than women aged 70 to 79 years.

Total energy intake declined, while the use of supplements and servings of fruits and vegetables increased with age (Table 3). There were no other important age-related differences in dietary factors. The small sample size for blood analytes precludes meaningful comparisons by age group (Table 4).

Racial/Ethnic Contrasts

The distributions of variables by ethnicity are shown in the appendix to Hays' article. The average age ranged from 60.6 years for Hispanic women to 63.9 years for White women. Hispanic women reported the lowest educational attainment, the lowest frequency of managerial/professional occupation, and the highest frequency of homemaker as sole occupation. Hispanics and American Indians had similar distributions of income, with nearly 40% reporting a family income below $20,000. In contrast, White women were 1.9 times more likely than American Indian and Hispanic, and 1.6 times more likely than Black women, to report family income above $50,000.

While few women in any of the ethnic groups had never married, Black women were less likely to be married currently than women of the other races/ethnicities. Previously married Black and Hispanic women were more likely to be divorced than widowed, while White and Asian women were slightly more likely to be widowed than divorced. Black women had the highest rates of living alone, divorce, and widowhood. Asian/Pacific Islander women were the least likely to live alone.

More Asian/Pacific Islanders reported never having been smokers than women of other races, while Black and American Indian women reported being current smokers more often than the other groups. White women reported a greater prevalence of alcoholic beverage use, and more frequent drinking than the other groups. White women engaged in substantially more moderate or strenuous activity than women in the other groups.

Black women had the highest prevalence of hysterectomy (54.8%). Black and American Indian women reported similar high rates of hysterectomy before the age of 40 (24.8% and 25.4%, respectively). Black and Hispanic women had substantially higher rates of tubal ligation (21.6% and 23.6%) than women of other races. The percentage of women ever breastfeeding was highest among Asian/Pacific Islanders (62.2%), and lowest among Blacks (47.7%). Benign breast disease was most common in Whites (23.0%) and least frequent in Hispanics (17.5%).

Over 60% of White and Asian/Pacific Islander participants were current or past users of postmenopausal hormones. Duration of use was greatest in Whites and Asian/

Table 3. Dietary intake of WHI Observational Study participants by age, from a Food Frequency Questionnaire

	Age at screening (y)							
	50–59 (N = 28,487)		60–69 (N = 39,640)		70–79 (N = 21,789)		Total (N = 89,916)	
Nutrient[a]	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
Energy (kcal)	28,487	1498 ± 563	39,640	1460 ± 531	21,789	1413 ± 512	89,916	1460 ± 537
Total fat (g)	28,487	50 ± 26	39,640	49 ± 25	21,789	48 ± 24	89,916	49 ± 25
% Energy from fat	28,487	30 ± 8	39,640	30 ± 8	21,789	30 ± 8	89,916	30 ± 8
Total carbohydrate (g)	28,487	189 ± 74	39,640	184 ± 69	21,789	180 ± 67	89,916	184 ± 70
Protein (g)	28,487	62 ± 26	39,640	61 ± 24	21,789	59 ± 24	89,916	61 ± 25
Total SFA (g)	28,487	17 ± 9	39,640	16 ± 9	21,789	16 ± 8	89,916	16 ± 9
% Energy from SFA	28,487	10 ± 3	39,640	10 ± 3	21,789	10 ± 3	89,916	10 ± 3
Total trans fatty acid (g)	28,487	2.9 ± 1.4	39,640	2.9 ± 1.4	21,789	2.9 ± 1.3	89,916	2.9 ± 1.4
Dietary fiber (g)	28,487	16 ± 6	39,640	16 ± 6	21,789	16 ± 6	89,916	16 ± 6
Cholesterol (mg)	28,487	173 ± 101	39,640	170 ± 98	21,789	161 ± 93	89,916	168 ± 98
Vitamin D (mcg)	28,487	4.1 ± 2.0	39,640	4.3 ± 2.1	21,789	4.4 ± 2.2	89,916	4.3 ± 2.1
Total alpha-toc eq (mg)	28,487	7.4 ± 3.0	39,640	7.5 ± 3.0	21,789	7.5 ± 3.0	89,916	7.5 ± 3.0
Vitamin C (mg)	28,487	94 ± 54	39,640	99 ± 54	21,789	104 ± 55	89,916	99 ± 54
Folacin (mcg)	28,487	228 ± 98	39,640	236 ± 97	21,789	238 ± 98	89,916	234 ± 98
Calcium (mg)	28,487	680 ± 372	39,640	675 ± 362	21,789	668 ± 363	89,916	675 ± 366
Total calcium (mg)	28,487	978 ± 611	39,640	1012 ± 618	21,789	1002 ± 611	89,916	999 ± 614
Fruits and vegetables (servings/day)	28,487	3.7 ± 1.6	39,640	3.9 ± 1.6	21,789	4.2 ± 1.7	89,916	3.9 ± 1.7
Grains (servings/day)	28,480	4.3 ± 1.8	39,633	4.0 ± 1.7	21,788	3.7 ± 1.5	89,901	4.0 ± 1.7

[a]Means and standard deviations were computed on the log scale and back-transformed values are reported.

Table 4. Baseline blood analytes from a random sample of WHI Observational Study participants by age

	Age at screening (y)								
	50–59 (N = 325)		60–69 (N = 453)		70–79 (N = 284)		Total (N = 1062)		Reliability (N = 564)
Blood Analyte[a,b]	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	ICC[c]
Total cholesterol (mg/dl)	325	210 ± 35.6	453	217.1 ± 34.9	284	220.3 ± 36.9	1062	215.4 ± 35.8	0.82
LDL-C (mg/dl)	316	115.8 ± 34	444	120.8 ± 33.6	282	125.3 ± 35.4	1042	120.4 ± 34.3	0.83
HDL-C (mg/dl)	324	60.2 ± 17.2	453	62.9 ± 16.4	284	60.6 ± 16.1	1061	61.4 ± 16.5	0.89
HDL-2 (mg/dl)	313	18.5 ± 8.7	447	20.5 ± 9.3	273	19.9 ± 9.2	1033	19.7 ± 9.1	0.88
HDL-3 (mg/dl)	313	40.6 ± 9.7	447	41.5 ± 8.8	273	40.3 ± 8.7	1033	40.8 ± 9	0.86
Triglyceride (mg/dl)	325	130.5 ± 65.9	453	131.3 ± 60.8	284	136.1 ± 58.8	1062	132.1 ± 61.6	0.80
Lp(a) (mg/dl)	322	16.6 ± 18	453	17.7 ± 19.7	284	15.1 ± 16.6	1059	16.6 ± 18.2	0.95
Retinol (μg/ml)	325	0.6 ± 0.14	452	0.61 ± 0.14	284	0.61 ± 0.16	1061	0.61 ± 0.15	0.81
Alpha-carotene (μg/ml)	325	0.07 ± 0.07	452	0.08 ± 0.06	284	0.08 ± 0.06	1061	0.08 ± 0.06	0.73
Beta-carotene (μg/ml)	325	0.22 ± 0.2	452	0.26 ± 0.2	284	0.29 ± 0.25	1061	0.26 ± 0.22	0.84
Beta-cryptoxanthine (μg/ml)	325	0.07 ± 0.05	452	0.08 ± 0.05	284	0.09 ± 0.06	1061	0.08 ± 0.06	0.62
Lycopene (μg/ml)	325	0.4 ± 0.22	452	0.36 ± 0.2	284	0.33 ± 0.21	1061	0.36 ± 0.21	0.65
Lutein and zeaxanthin (μg/ml)	325	0.19 ± 0.09	452	0.21 ± 0.1	284	0.22 ± 0.1	1061	0.21 ± 0.1	0.83
Alpha-tocopherol (μg/ml)	325	15.1 ± 5.7	452	17.2 ± 6.8	284	18.6 ± 7.4	1061	16.9 ± 6.7	0.81
Gamma-tocopherol (μg/ml)	325	1.4 ± 1.2	452	1.2 ± 0.9	284	1.2 ± 1	1061	1.3 ± 1	0.85
Factor VII activity, antigen (%)	309	126.2 ± 32.2	447	124.4 ± 29.7	273	121.1 ± 29.3	1029	123.7 ± 30.2	0.86
Factor VIIC (%)	299	121.5 ± 32	434	124.4 ± 29.1	268	122 ± 28.8	1001	122.6 ± 29.8	0.83
Fibrinogen (mg/dl)	309	286.7 ± 57.8	445	292.4 ± 55.5	274	298.5 ± 58.1	1028	292.1 ± 56.7	0.67
Glucose (mg/dl)	322	94.4 ± 19.2	452	93 ± 14.1	281	96.6 ± 18.8	1055	94.3 ± 17	0.83
Insulin (μIU/ml)	309	8.9 ± 4.6	428	8.5 ± 4	270	9.1 ± 4.6	1007	8.8 ± 4.3	0.71

[a]Means and standard deviations were computed on the log scale and back-transformed values are reported.
[b]Means and standard deviations are weighted by the overall CT & OS ethnic distribution.
[c]Intra-class correlation coefficient.

Pacific Islanders. Self-reported fracture at age 55 or older was twice as common in White (14.7%) compared with Black women (6.8%), with women of other races falling in between these rates. Hispanic women had the lowest rates of identifying a regular health care provider. Hispanic and American Indian women had the lowest rates of mammography within the past 2 years, or a PAP smear within the past 3 years, the highest prevalence of depression (23%), double the rate in Whites, and triple the rate in Asian/Pacific Islanders.

Systolic and diastolic blood pressures were greatest in Black women. The prevalence of treated hypertension in Blacks was 1.6 to 2.2 times greater than that of the other groups. American Indians were the most likely to have untreated hypertension. Black and American Indian women were more likely to have experienced a stroke or myocardial infarction. BMI was the lowest in Asian/Pacific Islanders and highest in Blacks; the mean BMI in all groups except Asian/Pacific Islanders was at least in the overweight range. The prevalence of diabetes was five times greater in American Indian, almost four times greater in Black and more than two times greater in Hispanic, than in White women.

Although White and American Indian women reported a previous diagnosis of cancer more often than women in the other ethnic groups, they did not have a striking excess of any specific type except melanoma. Black women had the highest rates of prior breast and colon cancers, while Asian/Pacific Islanders were the least likely to have had breast cancer.

Black women reported a relatively low total energy intake, but a high percent of energy from fat. White women reported low cholesterol consumption, and the highest consumption of energy, protein, carbohydrates, fiber, calcium, vitamin D, and fruit and vegetable servings.

Measurement Precision Study

Reliability statistics are shown in the final columns of Tables 1, 2, and 4. There were no major differences by age or ethnicity (data not shown). Most demographic factors, reproductive variables, and family medical history were reliably reported, with kappa or weighted kappa above 0.8. Occupation, years lived in the current state of residence, passive smoking exposure, physical activity and induced abortion had reliability coefficients in the 0.6 to 0.8 range. Most of the self-reported medical conditions yielded kappa above 0.75, however self-report for some medical conditions was not reliable at this level. These conditions included stroke, congestive heart failure, carotid endarterectomy/angioplasty, peripheral arterial disease, deep venous thrombosis, depression, and bone fracture at or after age 55. Reported number of falls in the last 12 months also had low reproducibility (kappa = 0.45), but part of this poor reliability is probably due to the shift in the 1-year reference period

between the first and second administration of the questionnaire.

Most blood analytes were reliable with ICCs above 0.8. Blood measures with less reliable ICCs (between 0.6 and 0.8), included insulin, fibrinogen and several of the serum carotenoids. Limited dietary sources of some of the carotenoids (e.g., lycopene) may make their serum levels more variable over time than for other nutrients.

Representative Relative Risks Demonstrable in Prospective Analyses

Applying conventional statistical assumptions of $\alpha = 0.05$ and $\beta = 0.80$, analyses in the entire OS population should allow demonstration of exposure:disease associations with a relative risk (RR) of 1.4 after 3 years, and well-below 1.25 after 6 years of follow-up for an exposure present in at least 10% of the population, e.g., hyperlipidemia, and a disease with an annual incidence of 5 per 1000, such as coronary heart disease (CHD) in women aged 70 to 74 years. An equivalent RR could be demonstrated after 3 years for an exposure present in at least 30% of the population, e.g. hypertension. For a less common disease with an annual incidence of 1 per 1000, e.g., breast cancer at ages 65 to 79 or CHD at ages 55 to 59, the detectable relative risks after 3, 6, and 9 years of follow-up for an exposure found in at least 30% of the population, e.g., high fat diet, are 1.5, 1.4 and 1.25, respectively.

At the other end of the spectrum, for analyses restricted to a sub-population of 6,000 participants, e.g., ethnic subgroups, demonstrable RRs at 3, 6, and 9 years for a risk factor with 10% exposure and a disease with 5/1000 annual incidence, are 2.75, 1.9, and 1.75, respectively. These estimates improve to 1.9, 1.65, and 1.4 if the exposure is present in 30% of the population. For a disease with 1/1000 annual incidence and a risk factor with 10% exposure, a RR of 3.2 is detectable at 9 years. If the exposure is present in 30% of the population, the detectable RR is 2.8 at 6 years and 2.5 after 9 years.

DISCUSSION

The fraction of the US population comprised of ethnic minorities decreases with age and this is reflected in the composition of the WHI OS cohort. According to US Census data for women aged 50 to 59, 60 to 69, and 70 to 79 years, the fraction of Blacks declines from 11% to 10% to 8%, and the fraction of Hispanics from 7% to 6% to 4%, while the fraction of Whites increases from 78% to 81% to 85% (4). The trends in the OS are similar but the minority fractions are slightly lower in each decade. Overall, 81% of US women aged 50 to 79 years were White, and the fraction in the OS is similar at 83%. While the cohort overall is somewhat better educated than same aged women in the US, OS volunteers are less different from the US population in general than participants in other recent studies of postmenopausal women (5,6).

Women enrolled in the OS have some traits that result from the clinical trial exclusions. Although its benefit remains to be proven, postmenopausal hormone use was popular as a preventive intervention for coronary disease when women were recruited to the WHI, and few women who were taking hormones were willing to participate in a randomized trial of this treatment. Thus, more OS women were on hormones at baseline than clinical trial participants. Other studies have found that women who elected to take hormones generally had more favorable risk factor profiles and healthier lifestyles than women who did not, even before they began using hormones (7–9).

Similarly, potential participants were excluded from the dietary modification trial if their diets were already low in fat. If they did not join the PHT trial, women excluded from the DM trial for this reason were offered participation in the OS. Eating a low fat diet is a common healthy behavior that may overlap with other healthy life style traits. Thus, because of the selection process for both the dietary and hormone trials, the OS would be expected to have more women with healthy life styles than the clinical trial and this is indeed the case.

Consistent with other US population data (10), total family income declined with increasing age. Some of this effect may be attributable to the parallel increase in widowhood and living alone. It is also possible that there is a cohort effect due to inflation, since wages were lower when the oldest participant's households were employed, which could influence the current value of savings. In census data from 1990 that were unselected for gender, the prevalence of total family income <$15,000 rose steeply from 5% to 37% as householder age went from between 45 and 54 years to between 65 and 74 years. Corresponding rates for income >$50,000 were 40% and 13% (10).

The trends in parity by age may be attributable to the social and economic trends during the reproductive years for these women. The oldest participants were in their childbearing years during World War II and the post-war baby boom, while the younger participants came of age when women were increasingly involved in the workplace. Oral contraceptives became available near the end of the reproductive years for the oldest women, but were an option throughout the reproductive years for the youngest.

As expected, the prevalence of hypertension increased with age in parallel with the age-related increases in systolic blood pressure. Yet, OS women may be healthier than the population from which they were drawn. For example, among NHANES-III women aged 50 to 79 years, 48%

AEP Vol. 13, No. S9
October 2003: S107–S121

were hypertensive, 7% reported a history of physician-diagnosed heart attack, and 5% reported a physician-diagnosed stroke (11). Equivalent rates in the OS were 34%, 3%, and 2%. Thus, the prevalence of coronary disease and stroke was only about half that expected using NHANES-III estimates. The fraction of current smokers in the OS, at 6%, is one-third the 18% rate in NHANES-III. This may be related to a healthy volunteer effect.

The frequency of engaging in some form of exercise did not decline by age in the OS sample. Similar findings have been reported for women aged 50 to 79 years in the NHANES-III population (12). However, BMI declined and waist/hip ratio increased with age. It is not clear whether these differences are meaningful in terms of body-weight–associated disease risks. They may also represent changes in body habitus resulting from age-related changes in height and girth, including those related to osteoporosis. A similar trend for declining BMI with age has been reported in NHANES-III (13).

Yet, despite their generally healthy risk factor profiles and lower self-reported prevalence of cardiovascular disease, cancer prevalence in the OS group was higher than population estimates. Compared with the NHANES-III cohort, slightly greater proportions of the OS cohort reported having had a cancer other than skin cancer. Similarly, estimated prevalence rates of invasive cancer computed from the Connecticut SEER registry (personal communication), weighted to the age distribution of the OS women, are 30% to 70% lower for breast, colorectal, and endometrial cancer, and two to three times lower for melanoma or cervical cancer. The excess rates in the OS may be explained by the likelihood that cancer survivors were motivated to join the WHI but were excluded from the clinical trial. The three-fold excess of melanoma and cervical cancer reported by WHI women may reflect in-situ disease that would not appear in SEER, or confusion of non-melanoma skin cancers with melanoma and cervical dysplasia with cancer in self-report. Conversely, the rates of melanoma may be lower in Connecticut where the degree of sun exposure is less than in the US as a whole.

Hip fracture incidence rates have been reported in other populations from hospital discharge data. They increase exponentially with age in White women (1.63/1000 in 65-year-olds to 35.4/1000 in 95-year-olds) and less than exponentially with age in Black women (14). These data are consistent with the WHI finding of increased prevalence with age. The WHI ethnic differences in hip fracture are consistent with those reported elsewhere (14–16).

OS Black women had the highest prevalence of hysterectomy overall, and hysterectomy before age 40. In contrast, recent data from the National Hospital Discharge Survey (NHDS) do not show a difference by race in annual rates of hysterectomy (17), suggesting that this discrepancy may reflect past rather than current practice. Also, the NHDS diagnosis most often associated with hysterectomy was leiomyoma (fibroids) which was twice as common in Black compared with White women (17). Symptomatic fibroids may influence these differences since other published data show that Black women undergo hysterectomy for fibroids at an earlier age than White women (18). OS Black women were twice as likely as other participants to have never had a term pregnancy, suggesting an increase in both premature births and abortions. This is consistent with data showing an increased risk of prematurity among Black women (19). The higher rates of tubal ligation in OS Hispanic and Black women is consistent with the increased parity and abortion rates that we observed in these groups. Differences in the rates of breastfeeding may relate to cultural differences in the acceptability of this practice.

The prevalence of depression was greater in younger women despite the greater likelihood that older women are widowed or living alone. This observation may be partly explained by the greater contribution of minority women to the younger age group since Hispanic and American Indian women had a particularly high prevalence of depression. It is also possible that the scale measures stress more than depression (20) and that younger women are more stressed due to competing roles.

The Measurement Precision Study found that most risk factors were reliably reported, similar to findings by others (21). It also confirmed the reliability of most health conditions that will be followed in the OS. Notable exceptions were found for major cardiovascular endpoints, depression, and bone fracture at age 55 or older. Notwithstanding the lower reliability of self-report for specific prevalent diseases, incident events resulting in hospitalization for these conditions will be validated by medical record review. The reliability of most blood analytes was excellent, although insulin, fibrinogen, and carotenoids were less reliable than other measures. These reliability coefficients reflect the measurement error of using a single measure at one point in time, including the errors due to specimen handling, laboratory error and "within-subject" variation over a 3-month period but not long-term variability.

While a longitudinal study that depends on volunteers cannot be fully representative of the population from which it is drawn, the WHI OS includes a greater number of minority and economically disadvantaged women than have previously participated in any comparable study. The differences between ethnic groups, particularly the contrasts between Hispanic women and the other ethnic groups with regard to education, family income and reproductive history are striking, as are the contrasts between Black women and the other ethnic groups in cardiovascular risk and factors that lead to living alone.

The WHI OS, with its large sample size overall, minority representation comparable to US population levels by age, long duration, and large variety of exposure and outcome variables measured over time, offers unusual opportunities to study predictors of both common and uncommon health outcomes in postmenopausal US women.

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ELSEVIER

Outcomes Ascertainment and Adjudication Methods in the Women's Health Initiative

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INTRODUCTION

Establishing, defining, collecting, and classifying outcomes are critical activities in clinical research. The Women's Health Initiative (WHI) has both observational study (OS) and clinical trial (CT) components designed to examine simultaneously the impact of a number of factors on many of the major causes of morbidity and mortality in postmenopausal women. Thus, WHI outcomes cover a wide range of diseases, such as cardiovascular diseases, cancers, fractures, and some age-related illnesses.

Most previous clinical trials in women have examined the effects of a single intervention in a limited pathophysiologic area. As such, effects of the intervention in other areas have often not been carefully monitored. Observational studies have tended to examine a broader range of outcomes but often in less detail and in smaller numbers of individuals than does the WHI OS. In the WHI outcomes process, equal, unbiased, blinded ascertainment across the arms of the clinical trial has been given the highest priority.

The size and complexity of the WHI has offered many challenges to this effort. A concerted attempt has been made to maximize the use of available resources to monitor in detail the many possible outcomes related to the interventions. A complex system was developed to standardize data collection methods across 40 clinical centers following over 160,000 women. This paper describes the definition of WHI outcomes, outlines the process for ascertaining and classifying these health events in all components of WHI, and presents reliability results.

WHI OUTCOMES

Primary and secondary outcomes for the WHI are defined for each study component. The primary outcomes are those associated with the primary clinical trial hypotheses: coronary heart disease for postmenopausal hormone therapy (PHT), breast and colorectal cancer for dietary modification (DM), and hip fracture for calcium and vitamin D supplementation (CaD) (Table 1). Secondary outcomes are defined as those having substantial pre-existing scientific merit, supportive of the primary hypotheses, or of interest for safety monitoring. Data on a variety of other outcomes are being collected from hospitalization records. Additional secondary outcomes include other age-related conditions and quality-of-life measures, whose means of assessment will be described elsewhere.

WHI focuses on disease prevention and risk factors. Statistical analyses will typically involve time-to-event analyses. With this perspective, the emphasis within WHI is on capturing and adjudicating the first event of each type in each woman after enrollment. Subsequent events of the same type generally receive less scrutiny.

Definition of Outcomes and Evidence Required

Cardiovascular diseases. Hospitalized myocardial infarction, definite silent myocardial infarction, and coronary

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TABLE 1. Outcomes for each arm of the WHI Clinical Trial and Observational Study

Outcome	PHT	DM	CaD	OS
Cardiovascular				
Coronary heart disease	1°	2°	x	x
Stroke	2°	2°	x	x
Congestive heart failure	2°	2°	x	x
Angina	2°	2°	x	x
Peripheral vascular disease	2°	2°	x	x
Coronary revascularization	2°	2°	x	x
Venous thromboembolic disease				
Pulmonary embolism	2°	x	x	x
Deep vein thrombosis	2°	x	x	x
Total cardiovascular	2°	2°	x	x
Cancer				
Breast	2°	1°	2°	x
Colorectal	x	1°	2°	x
Endometrial	2°	2°	x	x
Ovarian	2°	2°	x	x
Total cancers	2°	2°	2°	x
Fractures				
Hip	2°	x	1°	x
Other fractures	2°	x	2°	x
Total fractures	2°	x	2°	x
Other				
Diabetes mellitus requiring therapy	x	2°	x	x
Death from any cause	2°	2°	2°	x

"1°" indicates primary outcome; "2°" secondary or safety outcomes; "x" ascertained.

death are combined to form coronary heart disease (CHD), the primary cardiovascular outcome in WHI.

The WHI algorithm for classifying hospitalized myocardial infarction (MI) includes elements of the medical history, electrocardiogram readings, and results of cardiac enzyme/troponin determinations, and is adapted from standardized criteria (1, 2). All available electrocardiograms from a hospitalization are used to evaluate ECG criteria. Cardiac enzyme and/or troponin levels are classified as normal, equivocal (greater than the upper limit of normal but less than twice the upper limit of normal), abnormal (≥ twice the upper limit of normal) or incomplete, based on the normal range at the corresponding hospital. When multiple enzyme determinations are available, the most abnormal results are used in classifying the event. MI events that occur during surgery or are aborted by thrombolytic therapy or procedures are included. Aborted MIs meet all the following criteria: 1) symptoms and ECG evidence for acute MI; 2) therapy is followed by resolution of ECG changes; and 3) all cardiac enzymes are within normal limits. The algorithm defines reported MI events as "definite", "probable", or "not an MI", as indicated in Table 2. Primary analyses of CHD will use both definite and probable MI events as outcomes.

In the clinical trial, CHD also includes silent MI events detected on serial electrocardiograms done at baseline and every 3 years. WHI uses the Novacode (3) algorithm to determine which participants had a silent myocardial infarction. Serial Novacodes 5.1 and 5.2 are classified as "definite silent myocardial infarction" and Novacode 5.3 and 5.4 are classified as "probable silent myocardial infarction." Only definite silent MIs are included in the definition of CHD. Silent myocardial infarction is not ascertained in the observational study.

Coronary death is defined as death consistent with coronary heart disease as the underlying cause, based on review of medical records and death certificate, and is subclassified as:

Definite fatal MI. No known non-atherosclerotic cause and definite MI within 4 weeks prior to death.

Definite fatal CHD. No known non-atherosclerotic cause and one or both of the following: chest pain within 72 hours of death or a history of chronic ischemic heart disease (in the absence of valvular heart disease or non-ischemic cardiomyopathy.)

Possible fatal CHD. No known non-atherosclerotic cause and death certificate consistent with CHD as underlying cause.

TABLE 2. Criteria for the classification of myocardial infarction

	Cardiac Enzymes/Troponin			
ECG Pattern/Symptoms	Abnormal[a]	Equivocal[b]	Incomplete	Normal
Cardiac pain present				
Evolving Q wave and evolving ST-T abnormalities	Definite	Definite	Definite	Definite
Equivocal Q wave evolution; or evolving ST-T abnormalities, or new left bundle branch block	Definite	Definite	Probable	No MI
Q waves or ST-T abnormalities suggestive of an MI and not classified above	Definite	Probable	No MI	No MI
Other ECG, ECG absent or uncodable	Definite	No MI	No MI	No MI
Cardiac Pain absent				
Evolving Q wave and evolving ST-T abnormalities	Definite	Definite	Definite	Probable
Equivocal Q wave evolution; or evolving ST-T abnormalities; or new left bundle branch block	Definite	Probable	No MI	No MI
Q waves or ST-T abnormalities suggestive of an MI and not classified above	Probable	No MI	No MI	No MI
Other ECG, ECG absent or uncodable	No MI	No MI	No MI	No MI

[a]More than twice the upper limit of normal at the corresponding hospital laboratory. When multiple enzyme determinations are available, the most abnormal results are used in classifying the event.
[b]Greater than the upper limit of normal, but less than twice the upper limit of normal at the corresponding hospital laboratory.

AEP Vol. 13, No. S9
October 2003: S122–S128

Both hospitalized and out of hospital deaths due to coronary disease are included. It is recognized that when the cause of death is uncertain, the death certificate often lists coronary disease as the cause of death. Therefore, as in other studies, there will be some misclassification of cause of death, including the possibility that fatal pulmonary embolism may be misclassified as coronary death. Coronary disease deaths are subclassified as definite or possible, depending upon the level of evidence.

Table 3 briefly describes the WHI criteria for the secondary cardiovascular outcomes of stroke, congestive heart failure, angina, peripheral vascular disease, coronary revascularization, and the safety outcomes of deep venous thrombosis and pulmonary embolism. For the outcomes of angina, congestive heart failure, stroke, and peripheral vascular disease, only events requiring hospitalization are considered outcome events for WHI. Angina or congestive heart failure managed in the outpatient setting is not included as an outcome since the quality of data and the projected numbers of potential events with records available only in physicians' offices made monitoring these events impractical. It is anticipated that significant changes in clinical practice and in diagnostic technology are likely to occur during the study, however. For example, during the study thus far, the frequency of outpatient angioplasty (PTCA) has been increasing. Since it is important to identify all angioplasty procedures, self-reported outpatient angioplasty is documented as an outcome. Similarly, deep vein thrombosis is increasingly diagnosed and treated in the outpatient setting. While early in WHI this condition was ascertained only if it resulted in a hospitalization, it soon became clear that significant numbers of cases would be missed if outpatient-treated deep vein thrombosis were not included. Since 1999, both outpatient and inpatient cases of deep vein thrombosis are ascertained and adjudicated for participants in the PHT component.

TABLE 3. WHI criteria for angina, congestive heart failure, stroke, peripheral vascular disease, deep venous thrombosis, and pulmonary embolism

WHI outcome	Defining criteria
Stroke	Rapid onset of a persistent neurologic deficit attributed to an obstruction or rupture of the brain arterial system, lasting more than 24 hours and without evidence for other cause.
Congestive heart failure	Symptoms and signs consistent with congestive heart failure, plus: pulmonary edema by chest X-ray; or dilated ventricle or poor ventricular function by imaging studies; or physician diagnosis of congestive heart failure and receiving medical treatment.
Angina pectoris	Symptoms consistent with angina plus: revascularization procedure; *or* ⩾ 70% obstruction of any coronary artery; *or* ST-segment depression ⩾ 1 mm on stress testing or on resting ECG with pain; *or* positive scintigraphic or echocardiographic stress test; *or* angina diagnosed by physician and receiving medical treatment for angina.
Peripheral vascular disease	Disease that is symptomatic and/or requiring intervention, and located in the abdominal aorta, iliac arteries, or lower extremities.
Coronary revascularization	Documented coronary artery bypass graft (CABG) surgery or percutaneous transluminal coronary angioplasty (PTCA) or coronary stent or artherectomy
Deep venous thrombosis	Physician diagnosis of deep vein thrombosis of the lower extremity and positive findings on a diagnostic test.
Pulmonary embolism	Physician diagnosis of pulmonary embolism and positive findings on a diagnostic test.

Some cardiovascular disease outcomes may be underreported since WHI does not collect all possible outpatient-treated events. The lack of outpatient data will also complicate the task of identifying and classifying such events as angina, especially angina without coronary disease (coronary syndrome X) and congestive heart failure. Changes in treatment patterns, such as more aggressive treatment of women with angina, may also affect the rates of MI or other outcomes. For the clinical trial, there is no reason to expect differential ascertainment by study arm, thus bias is unlikely. For both the clinical trial and observational study, however, power to detect meaningful associations could be affected if a significant proportion of primary cardiovascular outcomes are treated in the outpatient setting in the future or by significant improvements in outcomes resulting from improved treatment. Trends in outpatient treatment will be followed through specific questions about cardiovascular diseases, so that self-reported events can be monitored. WHI collects information about medication use so that new uses of cardiovascular medications can be assessed. Outpatient treatment trends will be followed so that procedures can be adapted to include specific outpatient events if the benefits to the study are determined to outweigh the drawbacks of time and expense to the program.

Cancers. All invasive cancers are documented and coded according to primary site. Five main cancers (breast, colon, rectum, ovary, and endometrium) are coded for anatomic subsite, diagnosis date, extent of disease (stage, tumor size, laterality), tumor morphology (behavior, grade, histology) and estrogen and progesterone receptors (breast cancer only). Incident invasive and in situ (ductal and lobular carcinoma in situ) breast cancers, including second primaries, are ascertained and adjudicated. Incident invasive and in situ colon and rectal cancers are determined. Recurrent cancers are not included, but site-specific cancer deaths are recorded.

Since the diagnosis of some early cancers and cancer precursors is dependent on whether or not screening has

occurred, there is potential for over-reporting of diagnoses in some arms of the study, particularly the unblinded intervention arm of the Dietary Modification component. For this reason and for safety purposes in the Postmenopausal Hormone Therapy component, all clinical trial participants undergo regular screening mammograms as part of study protocol. Screening for colorectal cancer is not done in WHI. At each follow-up contact (semi-annually in the clinical trial, and annually in the observational study), however, information on screening procedures for colorectal cancer is collected, including: fecal occult blood testing, flexible sigmoidoscope, and colonoscopy. This will allow evaluation of rates of colon cancer according to the prevalence of screening.

The diagnosis of a main WHI cancer outcome is made if a pathology report substantiates a malignant primary invasive or in situ cancer of the breast, colon, rectum, endometrium, or invasive, in situ, or borderline (low malignant potential) ovarian cancer. All histologic types and anatomic subsites are included. A pathology report of invasive or in situ cancer also is used to confirm a self-reported diagnosis for other cancers (except non-melanoma skin cancers). Noncancerous colorectal polyps, atypical benign breast disease and other premalignant benign conditions are not adjudicated as WHI outcomes. Self-report of colorectal polyps and breast biopsies are collected for all components of WHI. All cancer related hospitalizations, surgeries, procedures, diagnostics or treatments for each first self-report of a malignant tumor are investigated. Cancer events can be documented with a pathology report from a diagnostic biopsy or from tissue obtained during surgical treatment. For the full coding of the cancer, however, pathology reports from diagnostic aspirations, biopsies, and surgeries, plus the discharge summary, are used. Both inpatient and outpatient cancer diagnoses are included.

Fractures. Fracture outcomes are those related to osteoporosis. Hip fracture is a primary outcome; other fractures (excluding fingers, toes, skull/facial bones, ribs, chest/sternum, and cervical vertebrae) represent a secondary outcome. The diagnosis of all fracture outcomes is based on the radiology report. Radiographs are not routinely obtained. For fractures, both inpatient and outpatient treated events are captured and adjudicated. All fractures are adjudicated in the clinical trial but only hip fractures are adjudicated in the observational study. Self-report of type of trauma is obtained from the participant for possible later exclusion of fractures due to motor vehicle accidents. Repeat occurrences of all fractures during follow-up are not investigated, however only repeat hip fractures are adjudicated.

Deaths. The underlying cause of death is classified on the basis of the death certificate, medical records, and other records such as an autopsy report. Evidence based on recent hospitalization and autopsy records is considered the most reliable for determining cause of death, and every effort is made to acquire such records. The death certificate diagnosis is used when no other records are available.

Outcomes Ascertainment

Potential outcomes are identified primarily through self-report at semi-annual contacts for clinical trial participants and annual contacts for observational study participants. Specific details of illnesses and hospitalizations are obtained as needed via a standardized questionnaire administered by phone or in-person interview, or self-completed form. For primary and secondary outcomes, portions of the medical record (discharge summary and results of relevant diagnostic and laboratory tests) are requested and assembled. These materials are provided to the designated local adjudicator who adjudicates the event. The WHI has set a goal that the ascertainment and adjudication of a WHI diagnosis at the clinical center be completed within 3 months of initial identification of a possible WHI outcome; the majority of WHI Clinical Centers meet this goal.

Following notice of a participant death, an attempt is made to obtain information on any outcomes occurring between the participant's last routine contact and her date of death. To ascertain survival and cause of death for all WHI participants, data linkage with the National Death Index of the National Center for Health Statistics will be performed several times during the study. WHI participants who are lost to follow-up or who are known to be dead will be matched to the National Death Index to search for otherwise unreported deaths and to ascertain causes of death.

Adjudication of Outcomes

Physicians in the Clinical Centers, the Clinical Coordinating Center, and the NIH classify WHI outcomes. In the first stage, the local Clinical Center physician adjudicator reviews the documents and assigns a diagnosis. All locally adjudicated primary and safety endpoint events of each trial component are then centrally reviewed. A fraction of locally adjudicated secondary endpoints are also referred for central adjudication for quality control purposes. The primary results for each clinical trial component will be based on data derived from central adjudication. To minimize potential bias in the ascertainment and classification of outcomes, WHI requires that local and central physician adjudicators not be exposed to any information that could result in potential unblinding, including participant contact or other aspects of the research record.

Local Adjudication

At each clinical center, the local physician adjudicator reviews the medical records and, using standardized criteria,

AEP Vol. 13, No. S9
October 2003: S122–S128

determines whether a WHI outcome has occurred and codes specifics of the diagnosis. Documents reviewed for cardiovascular diseases include the discharge summary, electrocardiograms, laboratory values, and diagnostic test reports. Materials collected for all of the cancer outcomes include the pathology report and hospital face sheet. Based on these documents the local adjudicator codes the primary cancer site based on ICD-O-2 codes (5), the date of diagnosis, and tumor behavior (invasive, in situ, borderline). The primary document for fracture adjudication is the radiologist's written report. Additional documentation for hip fracture includes the hospital discharge summary, and for other non-spine fractures includes emergency room, clinic and progress notes when a radiology report is not available. For cause of death, hospitalization records from the time of death and the most recent relevant hospitalization before death, as well as autopsy records and death certificate diagnoses are used. For many out-of-hospital deaths, the only documentation available is likely to be the death certificate. In these cases, the immediate and underlying causes of death are abstracted from the death certificate.

Central Adjudication

The primary and safety outcomes of each trial component, and all deaths in the clinical trial are centrally adjudicated. The purpose of central adjudication is to document and improve the accuracy of diagnoses, to provide continuity of diagnostic decisions in a study that is of longer duration than most clinical trials, and to serve as a source of ongoing training for local physicians. All occurrences of the five main cancers (breast, colon, rectum, endometrium, and ovary) are also reviewed centrally for additional coding.

Cardiovascular diseases. The Cardiovascular Central Adjudication Committee is responsible for review of the following WHI outcomes: MI, angina, congestive heart failure, coronary revascularization, coronary death, and for PHT component participants, pulmonary embolism and deep vein thrombosis. Angina, congestive heart failure, and revascularization are centrally adjudicated primarily to search for unreported MI. Strokes were later included in the list of centrally adjudicated outcomes for the PHT component. Other cardiovascular events that are adjudicated at the local level are not routinely centrally adjudicated, although samples of these events may be reviewed for quality control purposes. The central adjudicators complete coding forms that are identical to those used by the local physician adjudicators.

The Cardiovascular Central Adjudication Committee consists of 10 to 20 physician adjudicators from the clinical centers, the Clinical Coordinating Center, and the NIH. Central adjudicators from clinical centers do not centrally review their own clinic's cases. Early in the study, consensus on diagnostic standards was established in a series of face-to-face adjudication meetings. To reduce time requirements, travel burden, and administrative costs, a system of completing central adjudication by mail was initiated. Initially, two reviewers adjudicated each case and were asked to come to a consensus if they disagreed. If they could not agree, the full committee reviewed the case. The rate of agreement between the two central adjudicators was sufficiently high (94% agreement between the two central adjudicators on MI diagnoses among the first 94 cases of MI) that the system was modified to require only one central adjudication. A second central adjudicator is used to resolve discrepancies between the local and central adjudication. Face-to-face central adjudicator meetings are held as needed to review a sample of cases to ensure consistency of central adjudication and to train new central adjudicators.

Originally, central adjudication was planned to occur on a sampling basis (10% of events) after each local adjudicator had achieved 90% agreement with the central diagnosis on a minimum of 20 cases for a given diagnosis. The implementation of this sampling plan was significantly delayed by the limited number of events per adjudicator and turnover in the local adjudicators. To reduce the central adjudication workload to that originally projected, central adjudication will be required for all key cardiovascular events occurring in PHT participants and a random sample of similar events in the non-PHT participants.

Cancers. For all cases of the five main WHI cancers (breast, colon, rectum, ovary, and endometrium), documentation is sent to the Clinical Coordinating Center for centralized review and coding by trained cancer coders under the supervision of a cancer epidemiologist and physician. These documents include hospital discharge summary, operative reports, history and physical examination, radiology reports, oncology consultation reports, and estrogen and progesterone hormone receptor results for breast cancers. The purpose of the central cancer coding is to finalize each cancer outcome, record detailed characteristics of the cancer such as stage of disease, and review self-reported cases of the primary cancers that were denied by local adjudication.

Primary cancer site, anatomic subsite, diagnosis date, extent of disease (stage, tumor size, laterality), tumor morphology (behavior, grade, histology) and hormone receptor results (breast cancer only) are coded. Central cancer coding uses the SEER coding guidelines (6), which were chosen because they are likely to be relatively stable through the length of the WHI study (in contrast with TNM staging, which may change over time). Initially, a blinded, quality assurance sample was recoded by a different coder to determine inter-coder variability. Unusual or difficult-to-code cases are reviewed with a reference cancer pathologist who performs a similar function for the Seattle-Puget Sound SEER registry.

Fractures. All hip fractures are centrally adjudicated using the same criteria and documentation as used at the local adjudication step. Rarely, the central adjudicator may request the actual radiograph to confirm an equivocal hip fracture.

Deaths. Coding of deaths is difficult and prone to inaccuracies (7), especially when documents are lacking or are of poor quality. For this reason, initially two central adjudicators review all deaths and are required to come to agreement before a case is closed. A random sample of deaths is reviewed annually by the entire Cardiovascular Central Adjudication Committee.

Training

Clinical Center outcomes staff are required to attend initial central training on protocol, procedures, and changes in the health care environment that can impact WHI case documentation. Monthly regional conference calls are used for training and problem-solving. A national workshop provided supplemental training and problem-solving opportunities. Clinical Coordinating Center outcomes staff also conduct on-site training for clinics having problems with outcomes processing.

Local adjudicators complete a formal training process that includes reviewing the study protocol, policies, and procedures, and participation in a training conference call held semi-annually or as needed. Once trained, ongoing communication and feedback to all local adjudicators is maintained through a newsletter. Additional individual training is planned by providing local adjudicators with a review of common problems and difficult cases observed in the study-wide experience. Central adjudicators are trained during Cardiovascular Central Adjudication Committee meetings and through a mentor program, where they are paired with a more senior central adjudicator to review cases together.

RESULTS OF CLASSIFICATION PROCESS

The local adjudication results are shown in Table 4. For major outcomes, the agreement between self-report and local adjudicator diagnosis was good: the local adjudicator verified 91% of self-reported breast cancers and 81% of self-reported hip fractures. In contrast, the local adjudicator verified only 70% of self-reported MIs, although for 16%

TABLE 4. Local adjudication results for self-reported outcomes

				Not confirmed			
		Confirmed		Related outcome confirmed		No outcome found/ No documentation obtained	
	Self-reported N	N	%	N	%	N	%
Cardiovascular							
MI	631	444	70%	104	16%	83	13%
Stroke/TIA[a]	1032	790	77%	49	5%	193	19%
Congestive heart failure	425	293	69%	34	8%	98	23%
Angina[b]	1669	727	44%	216	13%	726	43%
Peripheral vascular disease	170	101	59%	20	12%	49	29%
Coronary revascularization	1260	1103	88%	90	7%	67	5%
DVT (PHT only)	129	83	64%	22	17%	24	19%
PE (PHT only)	58	52	90%	1	2%	5	9%
Carotid artery disease[b]	228	175	77%	33	14%	20	9%
Cancers							
Breast	1608	1471	91%	4	0%	133	8%
Colorectal	393	338	86%	22	6%	33	8%
Endometrial	195	140	72%	31	16%	24	12%
Ovary	150	106	71%	23	15%	21	14%
Other cancer[c]	1699	1183	70%	117	7%	399	23%
Fractures							
Hip	292	236	81%	10	3%	46	16%
Spine[d]	302	156	52%	13	4%	133	44%
Other	3011	2420	80%	22	1%	569	19%

[a]Stroke and TIA have a combined self-report. Only stroke is a WHI outcome.
[b]Angina that is self-reported after a first MI and carotid artery disease that is self-reported after a stroke has been confirmed are not adjudicated and these self-reports are not included in the table.
[c]Excludes non-melanoma skin cancer.
[d]Excludes fractures of the cervical vertebrae.

AEP Vol. 13, No. S9
October 2003: S122–S128

TABLE 5. Central adjudication results for locally confirmed outcomes

	Centrally adjudicated		
	Total	Confirmed	
Locally adjudicated outcome	N	N	%
Cardiovascular			
MI	403	351	87%
Angina	911	738	81%
Congestive heart failure	396	313	79%
CABG/PTCA	748	727	97%
Deep vein thrombosis	70	66	94%
Pulmonary embolism	36	34	94%
Cancers			
Breast	332	320	96%
Invasive	258	237	92%
In situ	74	58	78%
Colorectal	101	95	94%
Endometrial	67	63	94%
Ovarian	36	32	89%
Fractures			
Hip	163	157	96%

of self-reported MIs, the physician identified a related cardiovascular outcome such as angina or revascularization.

Local and central adjudication results are in generally good agreement for all outcomes (Table 5). Often, angina and congestive heart failure occur in conjunction with MI. Disagreement on these two events, when there is agreement about the MI, is not considered a serious disagreement. The agreement between local and central adjudication for cause of death is very good for cancer but not as strong for cardiovascular and other causes (Table 6). A relatively high proportion of the disagreement occurs when local adjudicators select "other cardiovascular cause", or "unknown cardiovascular cause", while the central adjudicators identify a specific type of cardiovascular death (data not shown).

TABLE 6. Agreement rates between locally and centrally determined cause of death

	Central adjudication results						
		Cause confirmed		Related cause found		Other cause	
Cause of death as determined by local adjudicator	N	N	%	N	%	N	%
Cardiovascular	305	224	73%	42	14%	39	13%
Cancer	552	521	94%	19	3%	12	2%
Other known cause	181	133	73%	13	7%	35	19%
Unknown cause	30	10	33%			20	67%

DISCUSSION

The identification and classification of outcomes in WHI is complex and challenging for several reasons. First, within WHI there are three trial components as well as an observational study and each has different primary and secondary outcomes. Methods for ascertainment and classification of the various types of outcomes differ. The size and age distribution of the WHI population guarantees a substantial number of outcomes. There are many clinical centers (many with their own satellite clinics) collecting medical information from many local hospitals, clinics, and physicians' offices. Finally, during this era of increased interest in patient privacy, many institutions are setting stringent requirements regarding release of medical information to second parties such as medical researchers. Nevertheless, the WHI program will document a large and diverse number of outcomes in a high-quality and timely manner. The WHI continues to monitor the agreement rates between self-report and adjudicated outcomes. Data from the early experience indicate documentation and adjudication of most major WHI outcomes continue to be necessary to assure the quality of these critical data. The diversity and number of outcomes in WHI will provide a rich data source for many etiologic analyses covering a wide spectrum of diseases and health-related events in women.

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ELSEVIER

The Women's Health Initiative Recruitment Methods and Results

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INTRODUCTION

One of the most challenging aspects of the Women's Health Initiative (WHI) was the recruitment of more than 161,000 women for this long-term prevention trial and observational study. The WHI had many enrollment goals that made recruitment efforts formidable (1). These included the recruitment of postmenopausal women, a group seldom targeted for clinical trials; enrolling minority groups in at least the same proportion as they existed in the general population; and enrolling women willing to participate in a long-term (8–12 year) study. The success of the WHI in meeting these goals can be attributed to several factors: the experience gained from prior studies, such as the National Cancer Institute (NCI)-sponsored Women's Health Trial (2), the subsequent Women's Health Trial Feasibility Study in Minority Populations (3), and the Postmenopausal Estrogen/Progestin Interventions Trial (4); detailed planning by the WHI investigators; the dedication of recruiters, staff, and investigators at the clinical centers; and, a social and political climate that enhanced women's interest in health research.

Prior to the WHI, few large-scale prevention or clinical trials focused on postmenopausal women. Indeed, until recently, relatively little emphasis was placed on the recruitment of women of any age into such studies (5). However, during the last decade, a number of forces have come together to change this situation. The stance that women should be "protected" from biomedical research (6,7) has given way to the requirement that they be included so that more can be learned about their health care needs (8).

Likewise, there have been increased efforts to recruit members of racial/ethnic minorities into clinical and prevention trials. The barriers that have limited the participation of minorities in biomedical research have been reviewed in detail elsewhere (9–11). To ensure that the WHI findings would be as generalizable as possible to U.S. postmenopausal women, the study had to find ways to overcome these barriers and recruit a representative sample of minority women in this age group.

This article reviews the WHI study population and screening process, recruitment methods, and the results of the recruitment efforts. We describe the common and unique strategies developed by individual clinics to enroll women in their local communities and the national framework that supported these efforts. The implications of the success of these methods for future studies are also discussed.

STUDY POPULATION

Eligibility was defined generally for all WHI components with component-specific exclusion criteria. All women enrolled in the WHI were between 50 and 79 years old and were postmenopausal at the time of enrollment. Inclusion criteria were liberal in order to facilitate recruitment and enhance generalizability. In addition to age and menopausal status, eligibility criteria for the clinical trial (CT) and observational study (OS) included ability and willingness to provide written informed consent and an agreement to reside in the area for at least 3 years after enrollment.

A partial factorial design enhanced the efficiency of recruitment by allowing women to enroll in the postmenopausal therapy (PHT) component, the dietary modification (DM) component, or both. The observational study cohort was comprised primarily of women screened for the clinical trial who were found to be ineligible or unwilling to be randomized to either the PHT or DM component, but

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were still interested in participating in a long-term research study. Women enrolled in one of the clinical trial components were screened for eligibility and invited to join the calcium and vitamin D (CaD) component at their first or second annual clinic visits.

Table 1 presents the specific exclusion criteria for the three trial components and the OS. Eligibility was ascertained using a stepped approach. Most women were evaluated early in the process to minimize the screening effort and time spent by ineligible women and clinic staff. Clinical centers were allowed to organize and schedule the required data collection procedures to fit their own logistical constraints to improve efficiency. Thus, the order of data collection varied between clinics and the proportions excluded by each reason has limited interpretation.

CLINICAL CENTERS

Participants were recruited from areas surrounding forty clinical centers established primarily at major academic health centers in 24 states and the District of Columbia. (See, the appendix in Rossouw's article for a list of clinical center locations.) Recruitment areas included urban, suburban, and rural populations. The original plan anticipated 45 clinical centers, each of which was to enroll 1,267 trial participants and 2,222 OS participants (total clinical trial = 57,000; OS = 100,000). Only 40 clinical centers were ultimately funded, resulting in a need to enhance recruitment through some of these existing sites. This additional activity was supported contractually by giving centers the option to supplement their recruitment goals in increments of 25%. Sixteen clinical centers were formally approved for enhanced recruitment. Others participated informally with more modest increases in recruitment activities.

Though not a probability sample, enrollment of racial/ethnic minority groups proportionate to the total minority population of women between 50 and 79 years of age (18.2% according to the 1990 U.S. Census) was a high priority of the program. To achieve this representation of minorities, 10 (out of 40) clinical centers with expertise and access to specific minority groups (American Indian, Black, Asian American/Pacific Islander, Hispanic) were selected to serve as minority recruitment sites. These identified minority sites were expected to have a 60% minority enrollment, while other clinical centers were to enroll minorities in proportion to local demographics.

OVERVIEW OF THE RECRUITMENT AND SCREENING PROTOCOL

For most clinics, initial contact with potential participants was through a mass mailing of the recruitment brochure, which provided basic information on the WHI and contained a postage-paid return postcard to indicate interest in study participation. Trained telephone interviewers conducted additional eligibility screening with age-eligible women who returned cards or called the clinical center. A total of three clinic visits were conducted to enroll women in the clinical trial and at least one visit to enroll in the OS. Prior to the first screening visit, interested women were sent materials that included a cover letter, directions to the clinic, a study logo bag for their current medications and dietary supplements, several self-administered questionnaires, and instructions to prepare for a fasting blood draw.

At the beginning of the first screening visit, each woman was given general information about the WHI components and viewed an introductory video providing an overview of the study. An informed consent form was signed to cover initial screening activities, including processing of questionnaire data, drawing blood, and obtaining medical records. Questionnaires were briefly reviewed (including dietary intake, behavioral measures, and medical, reproductive, and family histories) and brief physical examinations were conducted (anthropometric data). As the screening process continued, women received written materials and viewed videos about the components they were interested in joining and were asked to sign a consent form specific to each of these components. For those women progressing toward enrollment in the clinical trial, additional examinations and procedures were conducted as needed (including breast exams, food records for the DM, and a pelvic exam with endometrial aspiration and a placebo run-in for the PHT). At the final screening visit, eligible women were randomized by computer to intervention or control groups for each trial component they were joining.

Women could be found to be ineligible or unwilling for clinical trial enrollment at any point in the screening process. These women were offered the opportunity to participate in the OS and, if willing to join, completed OS enrollment activities at that time. In addition to those unable to join the clinical trial, several clinics recruited specifically for the OS toward the end of the recruitment period. Throughout the screening process, women had the opportunity to discuss the study and the specific components with clinic staff and to ask related questions. A more thorough description of the flow of screening activities used to recruit participants has been published (12).

RECRUITMENT METHODS

Local Clinical Center Activities

The responsibility for recruitment rested in the hands of the individual clinical centers. Each was given the latitude to

TABLE 1. WHI inclusion and exclusion criteria

Component	Inclusion criteria	Exclusion criteria
Clinical trial and observational study	50–79 years of age Postmenopausal If age ⩾55, no menstrual period for at least 6 months If age 50–54, no menstrual period for at least 12 months Ability and willingness to provide written informed consent (component specific) Intention to reside in area for at least 3 years	
Clinical trial and observational study		Competing risk: Any medical condition with predicted survival of <3 y Adherence or retention reasons: Alcohol or drug dependency Mental illness, including severe depression Dementia Active participation in other randomized intervention trial
Clinical trial		Competing risk: Any invasive cancer in previous 10 y Breast cancer at any time Mammogram or CBE findings suspicious of breast cancer MI in previous 6 months Stroke or TIA in past 6 months Chronic hepatitis or severe cirrhosis Safety reasons: Severe hypertension (systolic BP > 200 mm Hg or diastolic BP > 105 mm Hg) Severely underweight (BMI <18 kg/m^2) Hematocrit <32% Platelets <75,000 cells/ml Current use of oral daily corticosteroids Adherence or retention reasons: Unwilling to participate in baseline or follow-up examination components
Dietary modification (DM)		Adherence or retention reasons: Special dietary requirements incompatible with the intervention (e.g., celiac sprue) On a diabetic or low salt diet Gastrointestinal conditions contraindicating a high fiber diet Type 1 diabetes Colorectal cancer at any time Routinely eat ⩾10 meals per week prepared out of the home Unable to keep a 4-day food record FFQ percent calories from fat <32% FFQ energy intakes <600 or >5000 kcal Previous bilateral prophylactic mastectomy
Postmenopausal hormone therapy (PHT)		Safety reasons: Endometrial cancer at any time Endometrial hyperplasia Malignant melanoma at any time History of pulmonary embolism or deep vein thrombosis Previous osteoporosis-related fracture being treated with hormones History of bleeding disorder requiring transfusion History of hypertriglyceridemia Currently on anticoagulants Currently on tamoxifen Abnormalities in baseline pap smear, pelvic exam, or pelvic ultrasound Adherence or retention reasons: Severe menopausal symptoms that would make placebo treatment intolerable Inadequate adherence to placebo run-in Unable or unwilling to discontinue use of PHT or testosterone Refusal to have baseline endometrial aspiration
Calcium and vitamin D (CaD)		Safety reasons: History of renal calculi or hypercalcemia Current use of oral corticosteroids or calcitriol Intention to continue taking ⩾600 IUs of vitamin D per day

BMI, body mass index; BP, blood pressure; CBE, clinical breast exam; FFQ, food frequency questionnaire; PHT, postmenopausal hormone therapy; TIA, transient ischemic attack.

determine their own recruitment strategies, staffing patterns, clinic configuration, and visit flow. This level of flexibility was intended to allow each clinic to adapt the protocol to local strengths and constraints.

Staffing. Each center had a designated recruitment coordinator who served as the primary contact person within the study on recruitment-related issues. In most clinics, this person was responsible for local recruitment efforts, including mass mailings, community presentations, and media placement, but the training, scope, and level of responsibility varied between sites. At some centers, this person served as a supervisor to telephone interviewers, managing some aspects of data collection. Leadership of the recruitment team was clinic-dependent. At some sites, the principal investigator actively participated in all recruitment efforts. At others, the clinic manager provided oversight and direction, while the recruitment coordinator sometimes had overall decision-making authority.

Recruitment staff were trained to offer a friendly, caring, and nonjudgmental dialogue with potential participants. Designated minority recruitment centers made efforts to assure that the staff, especially those involved in recruitment, were configured to reflect the population of interest. For those centers recruiting heavily in Hispanic communities, access to bilingual recruitment staff was essential.

Local recruitment strategies. Most clinical centers in the WHI used multiple recruitment strategies, with mass mailings being the primary method of identifying interested potential participants for initial screening. The importance of multiple methods and the effectiveness of mass mailings have been documented in other studies that have recruited older adults to dietary and hormone therapy trials (13–16). Mass mailing represented the backbone of the WHI recruitment strategies because of its ability to reach the general population and its predictable load characteristics. Addresses for mass mailings were obtained from a variety of sources, including department of motor vehicle registration lists, voter's registration lists, driver's license lists, HMO enrollee lists, Health Care and Financing Administration (currently known as the Centers for Medicare and Medicaid Services) lists, and commercial mailing lists of age-eligible women. Many clinics also used enriched sources of potential participants, such as those participating in or found to be ineligible for previous clinical trials at their institutions. Most clinics (90%) used a professional mailing service to label, sort, and mail their brochures. Some used the brochure as a stand-alone mailer, while others added a cover letter, prescreening form, or interest survey.

Each clinic mailed an average of 1,000 to 5,000 brochures per month over a 3- to 5-year period, with some mailing up to 50,000 brochures in each of the final months. Individual clinics determined the frequency and quantity of mailings, which varied from weekly to quarterly, to maintain a steady flow of screening visits. Response rates (i.e., the number of women making contact for initial screening) varied across clinics and sources of mailing lists from less than 2% to approximately 20% for initial mailings, with somewhat lower rates for repeat mailings. Most centers repeated mailings to the same area several times (2–7 mailings to the same population) over the period of recruitment.

Mailings were supplemented by the following public awareness and recruitment strategies:

- Community presentations
- Local newspaper articles
- Newspaper ads
- Public service announcements (television and radio)
- Name-a-friend programs, soliciting referrals from enrolled participants
- Incentives (small gifts)
- Health fairs
- National and local press releases
- Physician/health care provider referrals
- Brochure placement in community (e.g., pharmacies, supermarkets, beauty salons, churches)
- Alliance building (meeting with women's groups such as sororities)
- Establishing community advisory boards for recruitment, brainstorming, contacts
- Mailings to physicians to request referrals

The strategies employed varied from site to site. Some of the more unusual strategies included providing transportation to screening visits, enlisting the support of local celebrities, and flying an airplane pulling a WHI recruitment advertisement over a college football game. Not all strategies were equally effective, and no formal evaluations of these efforts were conducted on a study-wide basis. Nevertheless, anecdotal information may be illuminating. For example, most recruitment coordinators reported that asking physicians to make referrals yielded few or no referrals. However, many investigators believed that it was important to contact primary care physicians in the community to enlist their support of their patients' participation in the study. Most clinical centers felt it was important to increase the women's awareness of the study. They did this through the media (e.g., paid advertisements, public service announcements, feature stories, and interviews) and by speaking at local women's events. Women were not paid to participate in the study, but a few clinics provided small incentives (e.g., refrigerator magnet photo frames with the WHI logo) at enrollment and follow-up visits. Women who were enrolled were encouraged to "enroll a friend" to help spread the message in hard-to-reach populations.

Strategies used to recruit members of minority groups included presenting information at churches, social gatherings, and organizations frequented by members of these

groups, or meeting with tribal leaders to gain access to American Indian women. Emphasis was also placed on contacting organizations for seniors and placing ads and brochures in places most visible to the target age group. Accommodations were made to ensure that materials and visits were appropriate for the target populations, such as allowing extra time at screening visits, providing extra assistance for women with physical limitations, and using large-size print for all written materials. Many clinics created local advisory boards to generate support from the local community and provide a ready source of feedback for nationally and locally created recruitment materials.

The WHI did not mandate adherence to one recruitment technique, but rather allowed each clinic to determine the best ways to maximize results in their own communities with their own resources and ideas. Clinics also made independent decisions about clinic hours and locations. Some clinics were open on Saturdays, while others were open during at least one evening per week to accommodate women who worked during weekday hours.

Clinics made efforts to help women overcome obstacles to participation, including helping to create carpools and providing bus passes, providing child care for women with primary responsibility for grandchildren, and reimbursing women for all or part of their parking fees. To make participation easier for relatives, women living in the same household, or those living close to one another, clinical centers were allowed to randomize groups of two or more participants together to a study arm. This was to help overcome transportation difficulties and to make sure that women living in the same household were not randomized to different arms in the DM. Overall, 456 groups of two or more women were formed (the maximum number of women randomized together was four), resulting in a total of 941 DM participants selecting this option.

Clinics routinely called to remind participants of scheduled appointments, and follow-up calls were made if appointments were missed. Logs were maintained of all contacts and outcomes. Regular strategy meetings were held to review outcomes from previous activities and make adjustments or take new directions. Although much effort was placed on meeting recruitment goals, the long-term nature of the WHI and the expectation for active study participation made it very important to recruit women who would be likely to stay with the study through the end of the intervention and follow-up period. The ambitious recruitment goals and the need to enroll women without substantial barriers to long-term adherence created a natural tension within the clinics. This was addressed with varying levels of success across clinics, but was most effectively managed in clinics where there was active leadership in place from someone with broad responsibility for the success of the overall program.

Activities at the National Level

Numerous activities at the national level supported and monitored local clinic efforts and enhanced visibility and bonding study-wide. These efforts, provided by the National Institutes of Health (NIH), the Clinical Coordinating Center (CCC), the Clinical Facilitation Center (CFC, subcontractor to the CCC for many aspects of performance monitoring), and various study-wide committees, included centrally produced recruitment and screening materials, central training workshops and support for local recruitment staff, a national public awareness campaign, a toll-free recruitment telephone line, and input from advisory groups with expertise in select areas.

Central development of materials. Recruitment materials were developed and produced centrally for study-wide use at the local level. These materials included a recruitment brochure with a postage-paid postcard customized for each clinic; a consent video providing an overview of study requirements shown at initial screening visits; a recruitment video featuring interviews with study participants; screening, eligibility, and consent forms; and recruitment posters, flyers, and postcards. All study-wide recruitment materials included the WHI logo (a stylized depiction of the profiles of three womens' faces and the study title), the study colors (dark blue and bright purple), the toll-free telephone number, and the catch phrase ("Be part of the answer") to enhance visibility and identification of the study. Most of the printed materials could be customized and supplemented with local information.

Spanish versions of all recruitment materials, including the videos and study logo, were available. Women of various ethnic backgrounds were included in videos, posters, and brochures. Special materials were developed to address specific study needs as they arose. For example, when recruitment goals for the younger age groups and the DM trial were met, special recruitment materials were developed specifically for the PHT and CaD trials targeting women over age 65. These included component-specific brochures and a letter from the director of the NIH.

Central training and support of local staff. Standard screening, consent, and eligibility procedures were developed at the national level and used across all clinics. Study-wide workshops were held annually for lead clinic recruitment staff during the recruitment period. These sessions provided the staff with an opportunity to share recruitment procedures and strategies and ensure that eligibility and screening procedures were consistent across clinics.

A full-time clinic recruitment staff liaison at the CCC provided general support for clinic recruitment activities by preparing recruitment progress reports, distributing materials and media placement information, assisting with obtaining mailing lists from the Health Care and Financing

Administration, and serving as a daily resource. Clinics had access to study-wide networking and support via monthly regional and national conference calls with recruitment staff from other clinics and the CCC recruitment liaison. The purpose of these calls was to disseminate information, share successful recruitment strategies, review recruitment progress reports, and provide moral support and encouragement. The WHI wide-area network provided a forum for ongoing e-mail communication and the dissemination of recruitment tips, strategies, and study updates in the form of a biweekly recruitment staff newsletter.

National public awareness campaign. During the second year of recruitment, a national public relations firm (Porter-Novelli) was enlisted to enhance study visibility and aid with national media placement and materials development. Over the course of 3 years, the firm developed English and Spanish print, radio, and television public service announcements (PSAs); distributed PSAs to national media outlets, resulting in placements in several widely circulated national magazines; assisted in the development of recruitment brochures, posters, and "invite a friend" postcards; produced consent and recruitment videos; distributed press kits and instructions to clinics for local media placement; and enlisted well-known celebrities (e.g., Angela Lansbury, Geraldine Ferraro) to serve as spokespersons and appear in recruitment materials. They also conducted focus groups and surveys of older women, incorporating these findings into materials and strategies. Altruism and the genuine desire to help other women seemed to be a theme that women identified with, since they understood that while study participation might not benefit them directly, the results would be helpful to future generations. This need to help other women and develop answers to women's health questions was reinforced in recruitment materials. The catch phrase "Be part of the answer" emphasized the idea that participants would be an important part of a group of women working together to find the answers to health questions facing all women.

Recruitment telephone line. A national toll-free telephone recruitment line (1-800-54-WOMEN) was established and maintained throughout the recruitment period. Women calling the number were automatically linked to the clinic nearest them. The CCC support person maintained the telephone line by collecting area code routing information from clinics. Women living outside of clinical center catchment areas were routed to the CCC and received a letter thanking them for their interest and a brochure listing the clinics and their locations.

Advisory groups. Early in the recruitment period, several committees comprised of WHI Investigators and staff members with specific expertise in areas such as special populations, clinic operations, and recruitment were formed. These committees were charged with identifying potential national recruitment efforts, reviewing all strategies and study materials, providing input on local recruitment strategies, managing the related clinical and operational aspects of recruitment, and providing recommendations toward increasing minority enrollment, including issues of cultural sensitivity.

Recruitment Monitoring

Recruitment progress was monitored centrally and locally throughout the recruitment period. To monitor overall recruitment progress and individual clinic performance, the CCC generated and distributed monthly reports depicting the expected and actual cumulative enrollment by study component in a graphical format (Figure 1). The CCC also provided graphical reports showing enrollment by age, and by uterus status (for PHT trial), as well as detailed tabular data of monthly and cumulative enrollment by age and race/ethnicity for each of the study components, for each clinic, and for all clinics combined. These reports identified recruitment deficits as they arose, so that special efforts could be made to achieve goals for all components, age, and racial/ethnic groups.

A Performance Monitoring Committee (PMC), consisting of representatives from the CCC, the CFC, the NIH, and the clinical centers, monitored recruitment progress throughout the enrollment period. The PMC reviewed each clinic several times per year to assess the clinic's progress in reaching their overall goals, as well as those for the age categories, study components, and minority groups.

Clinical centers that did not meet their goal after a reasonable interval were provided with varying levels of guidance and intervention to assist the center in achieving goals. A recruitment spreadsheet and associated catch-up plan was developed and provided to each clinic. This tool allowed them to estimate the level of mailings required to achieve their goals based on the clinic-specific recruitment record to date and other local level parameters such as stage-specific yields. For centers experiencing continuing difficulties in meeting recruitment goals, the PMC conducted conference calls and, in some cases, team visits to assess the local efforts and provide guidance. These were followed up with written reports that included specific action plans. A consistent theme in these interactions was the need to establish a mass-mailing program with adequate tracking to estimate yields, and to feed this information back into the mailing program.

Recruitment Data Collection

Most clinics used a tracking system to calculate the yields from their mailings and other recruitment efforts, but the types of system and information tracked varied widely across sites. No study-wide system was implemented because of

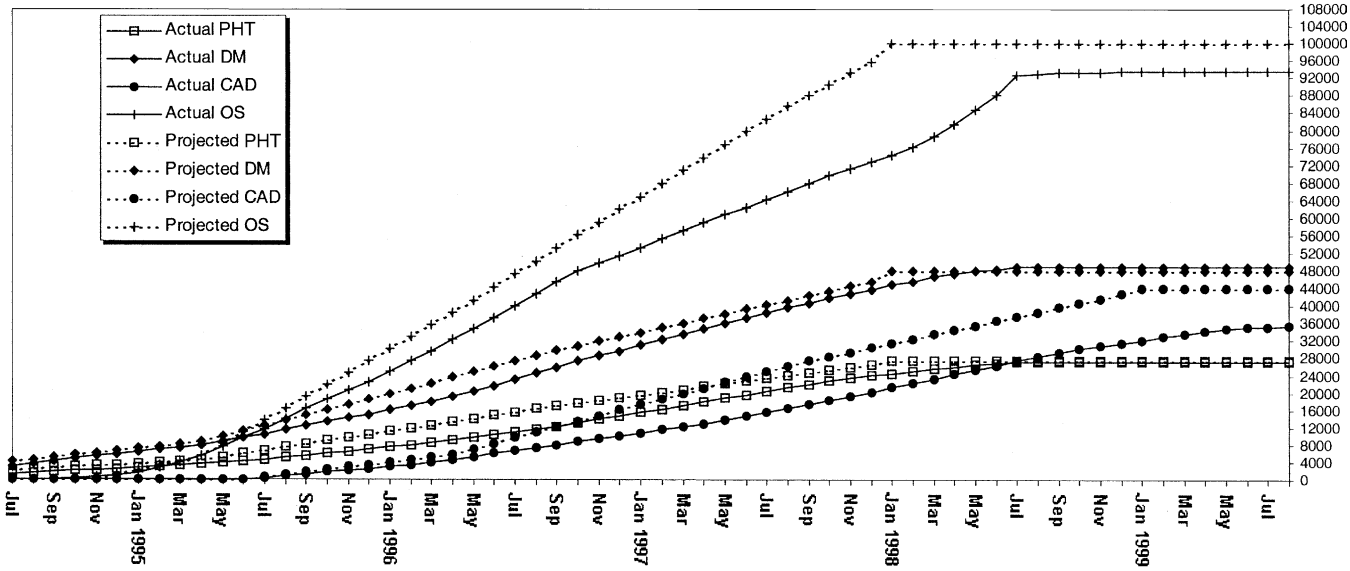

FIGURE 1. Projected and actual recruitment into WHI.

the clinic interests in maintaining as much local flexibility as possible. Therefore, total mailing numbers and response rates from mailings are not available across clinics. In addition, because each site could organize the screening process around their own strengths and constraints, the interpretation of step-by-step yields is not meaningful across sites. However, estimates of the yields from initial mailings and screening visits could be made for each center individually, based on their own mailing and enrollment numbers during the early months of recruitment. Using this information, clinics projected the number of mailings and screening visits needed per month to meet their specific goals by the end of the recruitment period. Based on overall estimates provided by clinics, approximately 3.2% of the recruitment mailings resulted in a contact with a potential participant to conduct initial screening activities.

In the context of initial screening, either by telephone or a self-administered questionnaire, potential participants were asked how they heard about the study and asked to select from one of the following: mailed letter/brochure, TV, radio, newspaper/magazine, meeting, friend/relative, other. These data were collected for all women screened, but clinics were not required to enter information for women who were determined to be clearly ineligible. Therefore, the total

TABLE 2. Study component recruitment by age and ethnicity

	Completed screening form (N = 373,092)	Randomized to clinical trial (N = 68,133)	Percentage of screened	Enrolled in observational study (N = 93,676)	Percentage of screened
Age at screening					
<50	961				
50–54	52,539	9,190	17.5	12,386	23.6
55–59	71,347	14,663	20.6	17,319	24.3
60–69	159,321	31,390	19.7	41,197	25.9
70–79	88,280	12,890	14.6	22,774	25.8
>79	100				
Missing	544				
Race/ethnicity					
American Indian	1,909	293	15.4	422	22.1
Asian	8,954	1,521	17.0	2,671	29.8
Black	34,578	6,988	20.2	7,639	22.1
Hispanic	15,116	2,889	19.1	3,623	24.0
White	300,445	55,521	18.5	78,013	26.0
Unknown	12,090	921	7.6	1,308	10.8

number of women screened for the WHI is not known, and total yields of each method based on the number screened are overestimated; however, because most women aged 50 to 79 were eligible for the OS, most clinics routinely entered these data.

RESULTS

The number of women with WHI screening data and the proportion of those randomized or enrolled in the clinical trial and OS by age and ethnic group are provided in Table 2. A total of 373,092 women completed the initial screening form. Of those, 68,133 (18%) went through the subsequent screening visits to be randomized into the clinical trial, and 93,676 (25%) were enrolled in the OS. Women in the oldest age group (70–79 years of age) had the lowest proportion of women randomized to the clinical trial after completing initial screening. There was little variability across age groups in the proportion of those screened that enrolled in OS. There was little racial variability in the proportion of women who were randomized to the clinical trial after completing an initial screening form, with 20% of Black, 19% of Hispanic, and 18% of Caucasian women completing the randomization process. Asian women (30%) were the most likely to be enrolled in the OS after entering the screening process.

Source of Information about WHI

Table 3 shows the reasons for initial contact with the WHI by enrollment status, and the age, race, and regional breakdowns for women who were enrolled or randomized in one of the study components. The majority of women (66.7% overall) indicated that they heard about the WHI through a mailed letter or brochure. Reading about the WHI in a paper or magazine was the next most common source of information about WHI (14.0% overall), followed by hearing about the study from a friend or relative (8.3%). There were no major differences between women who enrolled in the clinical trial versus the OS versus those who were not enrolled in either component.

There were several variations in sources of information about WHI by age group, race, and region. While a mailed letter or brochure was the most frequent response for all age groups, a higher percentage of women in the 70–79 category (70.3%) selected this source of information compared with women in the younger age groups (65.3% for those 60–69 and 55.1% for those 50–59). Women in the youngest age group were more likely to mention a TV or radio advertisement than were women in the two older age groups.

The media selected most often by women of all racial backgrounds was a mailed letter/brochure, while the second

TABLE 3. Type of initial contact with WHI by enrollment status, age, race, and region among enrolled/randomized respondents

		Mailed letter/brochure		TV		Radio		Newspaper or magazine		Meeting		Friend/relative		Other	
		Row %	Column %	Row %	Column %	Row %	Column %	Row %	Column %	Row %	Column %	Row %	Column %	Row %	Column %
All	All Responders (N = 364,720)[a]	66.7	—	3.3	—	1.1	—	14.0	—	0.9	—	8.3	—	5.7	—
	Not enrolled (56.6%)	69.5	58.6	3.3	56.1	1.1	55.1	12.8	51.5	0.7	43.7	7.2	49.1	5.3	51.9
	OS enrolled (25.1%)	62.1	23.6	3.0	22.9	1.1	24.2	15.8	28.7	1.3	35.3	10.2	31.1	6.6	29.0
	CT randomized (18.3%)	64.2	17.8	3.7	21.0	1.3	20.6	15.0	19.8	1.0	21.0	8.9	19.8	5.9	19.1
Age	50–59 (33.6%)[b]	55.1	28.9	4.6	46.2	1.7	49.1	18.6	39.8	1.2	33.6	11.0	37.9	7.8	40.9
	60–69 (42.8%)	65.3	46.5	2.9	39.6	1.0	38.5	14.4	41.9	1.1	43.2	9.5	44.2	5.8	41.5
	70–79 (23.6%)	70.3	24.6	2.1	14.2	0.7	12.4	12.8	18.3	1.2	23.2	7.8	17.9	5.0	17.6
Race	American Indian (0.5%)	56.1	0.4	4.2	0.6	1.3	0.5	13.8	0.4	4.7	1.8	10.5	0.5	9.5	0.7
	Asian/Pacific Islander (2.5%)	74.7	3.1	1.2	1.0	0.3	0.6	10.7	1.8	0.9	2.0	6.8	1.8	5.5	2.3
	Black (9.3%)	60.4	8.6	3.9	10.6	0.8	6.4	8.1	4.7	1.6	12.8	10.6	9.9	14.5	20.6
	Hispanic (4.1%)	52.9	3.4	7.1	8.8	3.3	11.3	12.6	3.3	1.3	4.7	17.2	7.2	5.6	3.6
	White (82.2%)	63.4	83.4	3.1	78.0	1.1	80.2	16.6	88.9	1.1	77.8	9.3	79.8	5.4	71.1
	Unknown (1.3%)	65.2	1.2	3.2	1.1	1.1	1.0	13.0	0.9	1.1	1.0	7.2	0.8	9.3	1.7
Region in U.S.	Northeast (21.1%)	68.7	25.0	1.5	10.5	1.2	24.2	16.2	24.1	1.3	25.4	7.2	17.1	3.9	14.2
	South (23.5%)	51.3	20.9	5.7	44.4	1.2	27.1	14.8	26.2	1.4	31.2	12.6	33.5	12.0	49.1
	Midwest (21.8%)	65.4	23.0	3.5	23.4	1.6	30.4	15.4	22.0	0.9	17.5	8.9	20.5	4.3	15.2
	West (33.7%)	67.0	31.1	2.4	21.7	0.7	18.3	14.6	27.7	1.0	25.8	9.5	29.0	4.6	21.5

CT, clinial trial; OS, observational study.
[a]Overall, initial screening information was data entered for 373,092 women. Of those, 364,720 (97.8%) answered a question asking what prompted them to contact WHI.
[b]Percent of all who had responded to the question.

TABLE 4. Reasons for exclusion from WHI study components[a]

Component	Criterion for exclusion	Percentage of total ineligible[b]
PHT	No consent/not interested in PHT	81.2
	Clinic impression of ineligibility	4.8
	Stratum full or closed	4.6
	History of breast cancer	4.5
DM	No consent/not interested in DM	50.3
	FFQ percent calories from fat/energy intakes	41.9
	Stratum full or closed	11.0
	10+ meals away from home per week	5.3
	History of breast cancer	4.8
CaD	Not willing to limit use of vitamin D	73.0
	No consent/not interested in CaD	44.3
	History of kidney stones	13.1
	Clinic impression of ineligibility	5.8
OS	No consent/not interested in OS	76.6
	Stratum full or closed	9.9

CaD, calcium and vitamin D; DM, dietary modification; FFQ, food frequency questionnaire; OS, observational study; PHT, postmenopausal hormone therapy.
[a]Only includes reasons with >4% of total ineligible.
[b]A participant may be ineligible for more than one reason.

most frequent category varied. There were also slight regional variations in the source of information cited. Because each site determined their own mix of recruitment efforts based on their judgment of the potential effectiveness of the methods in the local population, this variation is a function of both the choice of approaches used in these populations as well as their effectiveness.

The age, race, and regional variations in reasons for contacting the WHI for the sample of women who ultimately enrolled in the clinical trial or OS were similar to women who were screened for, but did not join, the WHI (data not shown).

Reasons for Exclusion from Study Components

Table 4 presents the most common reasons for exclusion from each of the study components for women with screening data. For all components, lack of interest and/or signed consent was the primary reason women did not join that particular part of the study (50.3% for DM, 81.2% for PHT, and 76.6% for OS). For DM, almost 42% were ineligible based on initial dietary assessment; about 10% of women screened were ineligible for DM due to competing risk and fewer than 3% were ineligible for safety reasons. For PHT, ineligibility due to competing risk factors overall was around 10%; exclusion for safety reasons overall was also about 10%.

There are limitations to these data, including the fact that screening data were not entered for all women determined to be ineligible during initial screening. For those that were entered, further eligibility data were not collected once a woman was determined to be ineligible for a particular component; criteria screened late in the process are therefore lower than they might have been had they been screened at an earlier stage. Because there were variations across clinics in the timing of screening activities, these rates are an approximation.

Characteristics of the Recruited Population

Table 5 presents the demographic and personal characteristics of women who enrolled in each component of the WHI. The final clinical trial enrollment was 27,347 for PHT (99% of the goal), 48,836 for DM (102% of the goal), and 36,282 for CaD (81% of the goal); final enrollment in the OS was 93,676 (94% of the goal). Randomization goals were met or exceeded for each of the age categories in both the PHT and DM arms of the clinical trial with the exception of the 70–79 age group, which proved to be the most challenging recruitment task.

Minority women were recruited into the clinical trial in the same proportion (18.5%) as is found in the U.S. population (18.2%) for a total of 12,612 minority women. The OS fell short of the 18.2% goal by less than two percentage points (16.7%, n = 15,663). Except for Hispanics, proportional representation of minority groups (Black, American Indian, Asian/Pacific Islander) was close to the national distribution. On average, designated minority clinics enrolled 40% minorities, while nonminority clinics enrolled an average of 10%. Extensive descriptions of all CT and OS cohorts by race/ethnicity are provided in the appendix at the end of this article.

Approximately one third of women in the WHI have at least a college degree, with an additional 36–40% having some education after high school. Minority women were least likely to hold a college degree and most likely to have attended only 0–8 years of school (data shown in appendix at the end of this article). Income was lowest for the PHT sample and highest for women in the OS. A majority of women in all components were married or living as married at the time of enrollment, while nearly one third were divorced/separated or widowed.

Women in the WHI were more likely to be overweight or obese than normal or underweight at the time of enrollment. Based on a body mass index of 25 or greater, three quarters of the women in the clinical trial were overweight or obese, as were nearly 60% of women in the OS. More than 90% of women in each component, however, rated their current health as good or better.

Recruitment efforts were enhanced through the use of a partial factorial design allowing women to enroll in more than one of the clinical trial components. Overall, 53.3% of women in the clinical trial were enrolled in CaD,

TABLE 5. Baseline characteristics of WHI final enrollment participants

	PHT N = 27,347		DM N = 48,836		CaD N = 36,282		OS N = 93,676	
	N	%	N	%	N	%	N	%
Age at screening (y)								
50–54	3425	12.5	6958	14.2	5157	14.2	12,386	13.2
55–59	5402	19.8	11,041	22.6	8264	22.8	17,319	18.5
60–69	12,364	45.2	22,714	46.5	16,521	45.5	41,197	44.0
70–79	6156	22.5	8123	16.6	6340	17.5	22,774	24.3
Race/ethnicity								
American Indian	131	0.5	203	0.4	149	0.4	422	0.5
Asian/Pacific Islander	527	1.9	1107	2.3	722	2.0	2671	2.9
Black	2741	10.0	5266	10.8	3317	9.1	7639	8.2
Hispanic	1543	5.6	1854	3.8	1507	4.2	3623	3.9
White	22,027	80.5	39,760	81.4	30,153	83.1	78,013	83.3
Unknown	378	1.4	646	1.3	434	1.2	1308	1.4
Education								
0–8 years	708	2.6	576	1.2	527	1.5	1560	1.7
Some high school	1459	5.4	1639	3.4	1375	3.8	3288	3.5
High school diploma/GED	5643	20.8	8518	17.6	6673	18.5	15,121	16.3
School after high school	11,036	40.7	19,308	39.8	14,372	39.9	33,933	36.5
College degree or higher	8296	30.6	18,488	38.1	13,098	36.3	39,002	42.0
Family income								
<$10,000	1721	6.7	1783	3.9	1465	4.3	3916	4.5
$10,000–$19,999	4337	16.8	5294	11.5	4353	12.6	10,100	11.7
$20,000–$34,999	7315	28.3	11,315	24.6	8911	25.9	20,226	23.3
$35,000–$49,999	5276	20.4	9822	21.3	7302	21.2	17,429	20.1
$50,000–$74,999	4220	16.3	9549	20.8	6849	19.9	17,486	20.2
$75,000+	2941	11.4	8242	17.9	5546	16.1	17,608	20.3
Marital status								
Never married	1023	3.8	1970	4.1	1437	4.0	4390	4.7
Divorced/Separated	4812	17.7	7704	15.8	5724	15.8	14,727	15.8
Widowed	5453	20.0	7646	15.7	6012	16.6	16,290	17.5
Presently married/Living as married	15,929	58.5	31,293	64.4	22,962	63.5	57,805	62.0
Body mass index (BMI), kg/m^2								
Underweight (<18.5)	157	0.6	154	0.3	148	0.4	1107	1.2
Normal (18.5–24.9)	7107	26.1	12,503	25.7	9430	26.1	36,687	39.6
Overweight (25.0–29.9)	9533	35.1	17,387	35.8	12,955	35.9	31,463	34.0
Obesity I (30.0–34.9)	6183	22.7	11,198	23.0	8203	22.7	14,578	15.8
Obesity II (35.0–39.9)	2807	10.3	5048	10.4	3644	10.1	5451	5.9
Obesity III (≥40)	1405	5.2	2322	4.8	1715	4.8	3282	3.6
Perceived health status								
Excellent	4314	15.9	7616	15.7	6274	17.4	16,577	17.8
Very good	11,197	41.2	19,968	41.1	15,482	42.9	37,686	40.5
Good	9234	34.0	17,081	35.2	11,942	33.1	29,670	31.9
Fair	2259	8.3	3675	7.6	2271	63.3	8210	8.8
Poor	155	0.6	240	0.5	125	0.3	882	1.0

CaD, calcium and vitamin D; DM, dietary modification; OS, observational study; PHT, postmenopausal hormone therapy.

11.8% were enrolled in both DM and PHT, and 7.4% of clinical trial participants were enrolled in all three trials (data not shown). Table 6 displays the percent overlap across the three clinical trials. Nearly 30% of PHT participants were also in the DM and close to 59% were in CaD. In the DM trial, 16.5% were also in PHT and just over 50% were in CaD.

DISCUSSION

The WHI met recruitment goals, including reaching a diverse population of postmenopausal women. The recruitment experience of the WHI may provide several useful lessons for investigators undertaking randomized clinical trials with older women.

At the clinic level, several factors may have contributed to successful recruitment. First, making the clinic as accessible as possible to older women was crucial. For many clinics, this involved staffing a satellite clinic part- or full-time and providing parking and/or reimbursement for transportation costs. Having convenient clinic hours was also perceived to be important, as was making sure that the clinic was well-managed and staffed by competent and friendly staff members. Second, weekly monitoring of clinic recruitment goals was necessary, including close review of reports distributed from the CCC and yields from mailings and other recruitment activities. Third, while multiple recruitment methods were employed, the use of mass mailings was critical to reach the large numbers of women needed for WHI. Although most clinics tried other strategies, in the long run, all clinics relied on mass mailings as their primary recruitment method.

In addition to frequent internal and external monitoring, sharing recruitment strategies among and between clinics was also helpful. Although clinics often differed in the characteristics and responses of potential participants in their areas, many strategies were useful across regions and clinics. A recruitment brochure that targeted the PHT arm of the trial, for example, proved to elicit a good response rate in one clinic, and was shared on the monthly calls and frequent e-mails between recruitment coordinators in the local clinics and with liaison staff at the CCC. In addition, the second group of clinical centers was able to learn from the experience of the vanguard group, which had started recruiting 18 months earlier. When the second round of clinical centers was funded, they were assigned a vanguard center to provide advice and assistance to help them "ramp up" quickly to the recruitment task.

One of the potentially overlooked reasons for the WHI's successful recruitment was the women's awareness of the need for this research and their eagerness to participate. Participants repeatedly mentioned that they did not feel enough was known about women's health. Many of them experienced a need for answers to their own health questions (e.g., whether or not to take hormones), and they wanted their daughters and granddaughters to be better informed in the future.

All WHI materials were printed with the WHI logo using the WHI colors. Marketing experts commonly refer to this as *branding*, the development of an easily identifiable image associated with a product or service. The consistent use of visual images and verbal messages helped to create a WHI brand that was easily recognizable. The use of multiple and varied channels to communicate the WHI recruitment message helped participants identify with the idea that they were "part of the answer" to questions about women's health.

TABLE 6. WHI clinical trials: percent overlap between components

Component	*N*	PHT	DM	CaD	In all three components
PHT	27,347	100%	29.4%	58.8%	18.4%
DM	48,836	16.5%	100%	51.6%	10.3%
CaD	36,282	44.3%	69.5%	100%	13.8%
Total CT	68,133				

The partial factorial design allowed a large cost saving since there was overlap in many of the study procedures for the three trials. Women who were unwilling or ineligible for the clinical trial were invited to participate in the OS, which allowed this additional resource to be developed at very modest additional cost. In addition, the packaging of these components into one large program brought attention to the effort.

Not all efforts and clinics achieved equal success. Because the focus of study was not on the comparison of various recruitment strategies, it is not known whether the differences in recruitment success among the 40 clinics is due to clinic characteristics, their various recruitment strategies, or the unique characteristics of the clinic's community and region. Clinics varied on a multitude of categories, including sociodemographic characteristics of participants; urban, rural, or suburban settings; ethnic and minority makeup of participants; and the experience of the clinic in conducting large trials. Women differed by clinic and region on rates of exclusion. For example, women were more likely to already be on hormones in some regions, making them less likely to be interested in that arm of the study (which involved a 3-month wash-out, with only a 50% chance of being put on active hormones again). Women of some ethnic groups were less likely to be interested in the DM because of their own cultural dietary practices, while others were already following low-fat diets and were therefore ineligible.

The WHI encountered several challenges during the recruitment process, many of which were addressed on both the study-wide and local level. Early on, it became apparent that OS enrollment was exceeding that for the clinical trial, prompting a temporary hold on OS enrollment. Projections of end numbers for each trial component by age stratum necessitated early closure of younger age cells that were likely to become overrepresented and focused clinic efforts on the older age groups and the PHT trial component. For example, toward the end of recruitment, clinics used enriched mailing lists (such as Medicare lists) and placed stories in magazines with an older audience to target older women. To help compensate for lower accrual rates in the PHT trials, PHT-only mailings were used, especially

in areas with low current hormone use, and clinic staff members were encouraged to spend more time briefing potential PHT participants before asking them to make a decision.

Minority recruitment was somewhat more difficult and costly than anticipated for several reasons. Because minority women often have lower income levels, they may face more obstacles to participation than middle-class majority women. For example, minority women may have transportation difficulties, be caregivers for grandchildren or other family members, move more frequently, or have interrupted telephone service. If they are living at or below the poverty level, they may experience additional stresses and be less inclined to give their time and efforts for research purposes. Minority women may be less familiar with the medical establishment and the idea of research volunteerism, or they may be suspicious of the research process.

To meet the special challenges in recruiting women from minority populations, designated minority clinics were selected in geographic areas with large minority populations. Clinics that enrolled large proportions of minority participants required an average of 2.5 more staff members than the remaining clinics. The average staffing level across the study was approximately 15 full-time equivalents for a clinic enrolling 1,700 clinical trial participants and 2,200 OS participants. Overall, WHI clinics used about 0.5 additional staff/100 participants for every 10% minority participants enrolled. In addition, mailing volumes and costs were higher in minority clinics. Incentives were offered to clinics to compensate for additional effort needed to succeed in minority enrollment, and enrollment of minorities was extended by 6 months for the OS.

All clinics found it to be more difficult to recruit women in the 70–79 year age group than those in the younger age groups. Many of the issues facing minority participants also affected women in the older age groups because women tend to have less income and more obstacles to participating in research studies as they age. Women in the oldest age category were more likely to have health problems that limited either their eligibility or their ability to participate, to have transportation or other mobility problems, or to feel that they were too old to be of value to the study. Successful efforts to recruit older women included obtaining mailing lists of older women, contacting retirement and other groups with a high proportion of older members, and asking older women to recommend a friend. In addition, a campaign specifically targeting older women, including a special invitational letter to join the WHI from the director of the NIH, was conducted toward the latter part of the recruitment period.

Finally, recruitment for the CaD trial, into which participants were enrolled at their 1- or 2-year annual visit, proved more difficult than originally envisioned. Reasons for this included a feeling they were doing enough for WHI already; a reluctance to take an additional pill (for those in the PHT); an unwillingness to take pills (mostly DM participants) and/or reluctance to taking additional supplements (for those already taking supplements); and the perception that the CaD trial was not as exciting as the other two trials. To address these difficulties, additional emphasis was made to clinic staff regarding the importance of this component, a special CaD recruitment brochure was developed, and participants were given a second opportunity to join at the second annual clinic visit, resulting in an improvement in recruitment rates.

SUMMARY

The recruitment of women into the WHI stands as an important accomplishment in clinical research history. This study demonstrated that postmenopausal women of varied ethnic groups could be recruited in large numbers across the U.S. More than 161,000 enrolled in one or more components of the study. The complex study design included three nested clinical trials and an observational study, and allowed each woman to choose how she participated, from taking study pills to enrolling in a dietary modification program to participating at an observational level only. Study participation required at least a 3-year commitment of all participants, and participants are urged to stay with the study for the full follow-up period of 8–10 years. Multiple, intense, and overlapping recruitment strategies at the national and local levels were essential for achieving the recruitment goals of the study. Recruitment also required significant commitments of financial and personnel resources. Several strategies proved indispensable, especially mass and repeated mailings to potential participants. Other strategies were used to recruit older women and women from a variety of racial and ethnic groups. Many of the strategies developed and used in this study are applicable for future prevention trials.

APPENDIX: COMPREHENSIVE DISPLAY OF INFORMATION BY RACE AND ETHNICITY FOR THE CLINICAL TRIAL AND OBSERVATIONAL STUDY

Tables 1–20

APPENDIX TABLE 1. Baseline demographic and general health characteristics of WHI Estrogen + Progestin participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 56)			Asian/Pacific Islander (*N* = 363)			Black (*N* = 1124)			Hispanic (*N* = 888)			White (*N* = 13,945)			Total[a] (*N* = 16,608)		
Characteristic	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Age at screening (y)	56		60.5 ± 6.8	363		63.2 ± 7.4	1124		60.9 ± 6.9	888		59.6 ± 6.4	13,945		63.7 ± 7.1	16,608		63.3 ± 7.1
50–59	27	48.2		132	36.4		535	47.6		491	55.3		4254	30.5		5522	33.2	
60–69	21	37.5		153	42.1		445	39.6		320	36.0		6471	46.4		7510	45.2	
70–79	8	14.3		78	21.5		144	12.8		77	8.7		3220	23.1		3576	21.5	
Education																		
0–8 years	*	*		*	*		33	3.0		218	25.2		107	0.8		379	2.3	
Some high school	*	*		14	3.9		119	10.7		101	11.7		482	3.5		735	4.5	
High school diploma/GED	*	*		63	17.4		176	15.8		148	17.1		2778	20.0		3222	19.5	
School after high school	26	46.4		155	42.8		446	40.0		270	31.2		5434	39.2		6415	38.9	
College degree or higher	16	28.6		123	34.0		342	30.6		129	14.9		5073	36.6		5753	34.9	
Family income																		
<$10,000	*	*		14	4.1		131	12.4		219	28.2		470	3.5		857	5.5	
$10,000–$19,999	13	24.1		47	13.6		205	19.4		191	24.6		1851	14.0		2348	15.0	
$20,000–$34,999	16	29.6		67	19.4		265	25.0		171	22.0		3735	28.2		4316	27.5	
$35,000–$49,999	10	18.5		74	21.4		197	18.6		88	11.3		2924	22.1		3329	21.2	
$50,000–$74,999	*	*		81	23.5		163	15.4		68	8.8		2421	18.3		2773	17.7	
$75,000+	*	*		62	18.0		97	9.2		40	5.1		1848	13.9		2075	13.2	
Occupation																		
Managerial/Professional	17	32.7		115	33.8		385	39.6		154	20.3		4790	38.8		5524	37.6	
Technical/Sales/Administrative	13	25.0		130	38.2		221	22.7		153	20.2		3871	31.3		4454	30.3	
Service/Labor	16	30.8		70	20.6		285	29.3		271	35.8		2413	19.5		3108	21.2	
Homemaker only	6	11.5		25	7.4		81	8.3		179	23.6		1279	10.4		1600	10.9	
Body mass index (BMI), kg/m^2	56		29.8 ± 6.3	363		25.2 ± 4.5	1118		31.0 ± 6.7	882		29.5 ± 5.7	13,870		28.3 ± 5.8	16,520		28.5 ± 5.9
Underweight (<18.5)	0	0.0		7	1.9		*	*		5	0.6		102	0.7		118	0.7	
Normal (18.5–24.9)	12	21.4		198	54.5		191	17.1		178	20.2		4295	31.0		4940	29.9	
Overweight (25.0–29.9)	22	39.3		111	30.6		349	31.2		338	38.3		4925	35.5		5826	35.3	
Obesity I (30.0–34.9)	12	21.4		35	9.6		305	27.3		229	26.0		2825	20.4		3467	21.0	
Obesity II (35.0–39.9)	7	12.5		10	2.8		164	14.7		89	10.1		1190	8.6		1475	8.9	
Obesity III (≥40)	*	*		*	*		105	9.4		43	4.9		533	3.8		694	4.2	
Marital status																		
Never married	*	*		17	4.7		66	5.9		40	4.6		552	4.0		686	4.1	
Divorced/Separated	23	41.1		47	13.0		366	32.9		223	25.7		2077	14.9		2774	16.8	
Widowed	6	10.7		53	14.7		237	21.3		136	15.7		2656	19.1		3137	19.0	
Presently married/ Living as married	26	46.4		244	67.6		445	39.9		470	54.1		8625	62.0		9945	60.1	
Height (cm)	56		160.6 ± 6.2	363		154.7 ± 6.6	1120		162.5 ± 6.7	886		156.8 ± 6.5	13,902		162.1 ± 6.3	16,558		161.6 ± 6.6
Weight (kg)	56		76.7 ± 15.9	363		60.4 ± 12.2	1124		82.3 ± 18.9	886		72.7 ± 15.2	13,924		74.5 ± 16.3	16,585		74.7 ± 16.6
Waist/hip ratio (WHR)	55		0.84 ± 0.1	360		0.82 ± 0.1	1120		0.83 ± 0.1	884		0.82 ± 0.1	13,881		0.82 ± 0.1	16,532		0.82 ± 0.1
Waist (cm)	55		90.3 ± 14.9	361		79.5 ± 10.8	1121		92.1 ± 13.7	885		88.1 ± 12.6	13,903		87.8 ± 13.7	16,557		88.0 ± 13.8
Living alone																		
No	45	81.8		306	84.8		802	73.1		729	83.9		10,300	74.3		12,359	75.0	
Yes	10	18.2		55	15.2		295	26.9		140	16.1		3561	25.7		4115	25.0	
U.S. region																		
Northeast	6	10.7		19	5.2		224	19.9		105	11.8		3431	24.6		3834	23.1	
South	19	33.9		32	8.8		531	47.2		446	50.2		2936	21.1		4011	24.2	
Midwest	8	14.3		17	4.7		252	22.4		22	2.5		3868	27.7		4195	25.3	
West	23	41.1		295	81.3		117	10.4		315	35.5		3710	26.6		4568	27.5	

Smoking												
Never smoked	26	47.3	234	64.8	519	47.1	564	64.5	6711	48.7	8177	49.8
Past smoker	18	32.7	98	27.1	412	37.4	235	26.9	5676	41.2	6519	39.7
Current smoker	11	20.0	29	8.0	172	15.6	76	8.7	1405	10.2	1718	10.5
Alcohol intake												
Never drinker	*	*	134	37.1	185	16.6	208	23.8	1343	9.7	1910	11.6
Past drinker	16	28.6	66	18.3	325	29.1	190	21.8	2160	15.6	2807	17.0
<1 drink per mo	*	*	56	15.5	161	14.4	113	12.9	1924	13.9	2291	13.9
<1 drink per wk	16	28.6	52	14.4	215	19.3	180	20.6	2707	19.6	3223	19.6
1–<7 drinks per wk	10	17.9	39	10.8	188	16.9	153	17.5	3717	26.9	4151	25.2
7+ drinks per wk	*	*	14	3.9	41	3.7	29	3.3	1992	14.4	2096	12.7
Physical activity												
No activity	10	18.9	63	17.8	262	24.8	196	24.0	2199	17.2	2783	18.2
Some activity	26	49.1	165	46.6	505	47.9	384	46.9	5377	42.1	6556	42.9
2–<4 episodes per wk of moderate + activity	6	11.3	49	13.8	137	13.0	110	13.4	2087	16.3	2415	15.8
4+ episodes per wk of moderate + activity	11	20.8	77	21.8	151	14.3	128	15.6	3103	24.3	3512	23.0
Total expenditure/wk from physical activity (METs)												
0–1.5	12	22.6	83	23.4	348	33.0	268	32.8	3080	24.1	3855	25.3
>1.5–8	19	35.8	101	28.5	325	30.8	232	28.4	3510	27.5	4244	27.8
>8–19	13	24.5	97	27.4	220	20.9	191	23.3	3400	26.6	3981	26.1
>19	9	17.0	73	20.6	162	15.4	127	15.5	2776	21.7	3186	20.9
Total calcium intake (mg)												
0–<400	15	28.3	65	19.0	271	25.9	122	15.1	1009	7.4	1521	9.5
400–<800	11	20.8	118	34.5	394	37.7	296	36.6	3957	29.1	4832	30.1
800–<1000	9	17.0	36	10.5	123	11.8	102	12.6	1906	14.0	2203	13.7
1000–<1200	9	17.0	29	8.5	80	7.7	83	10.3	1600	11.8	1828	11.4
1200+	9	17.0	94	27.5	177	16.9	205	25.4	5109	37.6	5665	35.3
Any supplement use												
No	30	53.6	111	30.6	578	51.4	466	52.5	4895	35.1	6170	37.2
Yes	26	46.4	252	69.4	546	48.6	422	47.5	9050	64.9	10,438	62.8
Multivitamin use (with or without minerals)												
No	46	82.1	233	64.2	863	76.8	701	78.9	8715	62.5	10,717	64.5
Yes	10	17.9	130	35.8	260	23.2	187	21.1	5230	37.5	5890	35.5
Vitamin C as single supplement												
No	49	87.5	280	77.1	956	85.1	768	86.5	10,810	77.5	13,041	78.5
Yes	7	12.5	83	22.9	168	14.9	120	13.5	3135	22.5	3567	21.5
Vitamin E as single supplement												
No	46	82.1	263	72.5	931	82.8	739	83.2	10,409	74.6	12,564	75.7
Yes	10	17.9	100	27.5	193	17.2	149	16.8	3536	25.4	4044	24.3
Calcium as single supplement (including antacids)												
No	52	92.9	268	73.8	996	88.6	764	86.0	10,507	75.3	12,776	76.9
Yes	*	*	95	26.2	128	11.4	124	14.0	3438	24.7	3832	23.1
Single supplement (not Vitamin C, E, or calcium)												
No	46	82.1	222	61.2	874	77.8	664	74.8	9212	66.1	11,170	67.3
Yes	10	17.9	141	38.8	250	22.2	224	25.2	4733	33.9	5438	32.7
Any supplement (excluding single supplement calcium)												
No	32	57.1	126	34.7	617	54.9	498	56.1	5513	39.5	6887	41.5
Yes	24	42.9	237	65.3	507	45.1	390	43.9	8432	60.5	9721	58.5

[a]Total includes those of unknown ethnicity.
*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 2. Baseline demographic and general health characteristics of WHI Estrogen-Alone participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 75)			Asian/Pacific Islander (*N* = 164)			Black (*N* = 1617)			Hispanic (*N* = 655)			White (*N* = 8082)			Total[a] (*N* = 10,739)		
Characteristic	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Age at screening (y)	75		62.3 ± 6.7	164		63.2 ± 7.7	1617		61.6 ± 7.1	655		59.7 ± 6.5	8082		64.3 ± 7.2	10,739		63.6 ± 7.3
50–59	28	37.3		52	31.7		665	41.1		338	51.6		2179	27.0		3310	30.8	
60–69	35	46.7		73	44.5		699	43.2		263	40.2		3722	46.1		4852	45.2	
70–79	12	16.0		39	23.8		253	15.6		54	8.2		2181	27.0		2577	24.0	
Education																		
0–8 y	*	*		*	*		60	3.8		162	25.1		95	1.2		329	3.1	
Some high school	*	*		*	*		181	11.4		79	12.2		438	5.5		724	6.8	
High school diploma/GED	13	17.6		40	24.5		254	16.0		113	17.5		1970	24.5		2421	22.8	
School after high school	40	54.1		62	38.0		692	43.6		212	32.9		3551	44.2		4621	43.4	
College degree or higher	13	17.6		51	31.3		400	25.2		79	12.2		1971	24.6		2543	23.9	
Family income																		
<$10,000	11	15.5		10	6.3		253	16.8		143	25.0		439	5.7		864	8.5	
$10,000–$19,999	14	19.7		20	12.6		332	22.0		157	27.4		1431	18.7		1989	19.7	
$20,000–$34,999	16	22.5		37	23.3		421	27.9		129	22.5		2360	30.8		2999	29.7	
$35,000–$49,999	17	23.9		29	18.2		238	15.8		78	13.6		1564	20.4		1947	19.3	
$50,000–$74,999	*	*		35	22.0		174	11.5		48	8.4		1158	15.1		1447	14.3	
$75,000+	*	*		28	17.6		89	5.9		18	3.1		717	9.3		866	8.6	
Occupation																		
Managerial/Professional	18	27.3		54	35.1		452	32.7		103	18.4		2339	33.3		3006	32.2	
Technical/Sales/ Administrative	17	25.8		59	38.3		369	26.7		133	23.8		2329	33.1		2947	31.6	
Service/Labor	27	40.9		36	23.4		433	31.3		176	31.5		1632	23.2		2346	25.1	
Homemaker only	*	*		5	3.2		130	9.4		147	26.3		734	10.4		1035	11.1	
Body mass index (BMI), kg/m^2	73		31.2 ± 5.1	163		26.8 ± 5.5	1604		32.2 ± 6.8	647		30.5 ± 5.7	8040		29.7 ± 6.0	10,672		30.1 ± 6.2
Underweight (<18.5)	0	0.0		*	*		8	0.5		*	*		26	0.3		39	0.4	
Normal (18.5–24.9)	7	9.6		67	41.1		176	11.0		103	15.9		1784	22.2		2167	20.3	
Overweight (25.0–29.9)	26	35.6		49	30.1		502	31.3		235	36.3		2832	35.2		3707	34.7	
Obesity I (30.0–34.9)	23	31.5		30	18.4		450	28.1		186	28.7		2001	24.9		2716	25.4	
Obesity II (35.0–39.9)	12	16.4		11	6.7		263	16.4		79	12.2		951	11.8		1332	12.5	
Obesity III (≥40)	5	6.8		*	*		205	12.8		43	6.6		446	5.5		711	6.7	
Marital status																		
Never married	*	*		12	7.4		92	5.8		11	1.7		211	2.6		337	3.2	
Divorced/Separated	13	17.6		25	15.4		499	31.3		154	23.9		1316	16.3		2038	19.1	
Widowed	18	24.3		29	17.9		425	26.6		105	16.3		1712	21.3		2316	21.7	
Presently married/ Living as married	40	54.1		96	59.3		580	36.3		375	58.1		4816	59.8		5984	56.1	
Height (cm)	74		161.2 ± 6.5	163		154.7 ± 6.0	1606		162.4 ± 6.2	650		156.7 ± 6.5	8055		161.6 ± 6.3	10,693		161.3 ± 6.5
Weight (kg)	74		81.2 ± 15.2	164		64.8 ± 15.7	1615		85.1 ± 18.7	655		75.7 ± 16.2	8073		77.8 ± 16.8	10,727		78.6 ± 17.3
Waist/hip ratio (WHR)	74		0.85 ± 0.1	163		0.84 ± 0.1	1608		0.83 ± 0.1	652		0.83 ± 0.1	8058		0.83 ± 0.1	10,700		0.83 ± 0.1
Waist (cm)	74		95.7 ± 17.4	163		84.0 ± 12.7	1612		94.0 ± 13.4	653		90.8 ± 12.5	8063		91.3 ± 13.9	10,711		91.6 ± 13.8
Living alone																		
No	61	82.4		129	80.1		1108	69.8		537	83.8		5849	73.0		7794	73.4	
Yes	13	17.6		32	19.9		479	30.2		104	16.2		2166	27.0		2829	26.6	
U.S. region																		
Northeast	12	16.0		7	4.3		210	13.0		51	7.8		1815	22.5		2118	19.7	
South	22	29.3		8	4.9		876	54.2		338	51.6		1910	23.6		3175	29.6	
Midwest	12	16.0		11	6.7		396	24.5		32	4.9		2059	25.5		2526	23.5	
West	29	38.7		138	84.1		135	8.3		234	35.7		2298	28.4		2920	27.2	

Smoking												
Never smoked	36	50.0	107	66.0	784	49.5	396	61.1	4031	50.3	5428	51.1
Past smoker	30	41.7	44	27.2	590	37.2	190	29.3	3168	39.6	4075	38.4
Current smoker	6	8.3	11	6.8	210	13.3	62	9.6	807	10.1	1113	10.5
Alcohol intake												
Never drinker	14	18.9	53	32.7	306	19.2	161	25.1	891	11.1	1455	13.7
Past drinker	18	24.3	48	29.6	543	34.0	157	24.5	1741	21.7	2547	23.9
<1 drink per mo	14	18.9	23	14.2	201	12.6	101	15.7	1174	14.6	1533	14.4
<1 drink per wk	*	*	26	16.0	279	17.5	112	17.4	1607	20.0	2050	19.3
1–<7 drinks per wk	13	17.6	*	*	201	12.6	85	13.2	1785	22.3	2118	19.9
7+ drinks per wk	*	*	*	*	65	4.1	26	4.0	819	10.2	932	8.8
Physical activity												
No activity	10	14.1	29	18.5	377	25.0	175	29.0	1509	20.7	2124	21.7
Some activity	37	52.1	80	51.0	713	47.2	291	48.2	3286	45.0	4485	45.8
2–<4 episodes per wk of moderate + activity	7	9.9	24	15.3	203	13.4	64	10.6	1107	15.2	1428	14.6
4+ episodes per wk of moderate + activity	17	23.9	24	15.3	218	14.4	74	12.3	1398	19.2	1747	17.9
Total expenditure/wk from physical activity (METs)												
0–1.5	17	23.9	44	28.0	522	34.5	234	38.7	2075	28.4	2925	29.9
>1.5–8	19	26.8	45	28.7	460	30.4	180	29.8	2227	30.5	2982	30.5
>8–19	20	28.2	41	26.1	331	21.9	126	20.9	1781	24.4	2331	23.8
>19	15	21.1	27	17.2	198	13.1	64	10.6	1217	16.7	1546	15.8
Total calcium intake (mg)												
0–<400	8	11.9	36	23.7	432	29.0	103	16.9	828	10.6	1437	14.0
400–<800	22	32.8	51	33.6	585	39.3	206	33.7	2536	32.5	3452	33.7
800–<1000	12	17.9	20	13.2	140	9.4	75	12.3	1075	13.8	1342	13.1
1000–<1200	7	10.4	15	9.9	120	8.1	65	10.6	855	11.0	1077	10.5
1200+	18	26.9	30	19.7	211	14.2	162	26.5	2502	32.1	2942	28.7
Any supplement use												
No	27	36.0	59	36.0	875	54.1	344	52.5	3130	38.7	4491	41.8
Yes	48	64.0	105	64.0	742	45.9	311	47.5	4952	61.3	6248	58.2
Multivitamin use (with or without minerals)												
No	53	70.7	112	68.3	1259	77.9	507	77.4	5269	65.2	7301	68.0
Yes	22	29.3	52	31.7	358	22.1	148	22.6	2813	34.8	3438	32.0
Vitamin C as single supplement												
No	57	76.0	120	73.2	1405	86.9	552	84.3	6388	79.0	8636	80.4
Yes	18	24.0	44	26.8	212	13.1	103	15.7	1694	21.0	2103	19.6
Vitamin E as single supplement												
No	61	81.3	117	71.3	1404	86.8	557	85.0	6199	76.7	8444	78.6
Yes	14	18.7	47	28.7	213	13.2	98	15.0	1883	23.3	2295	21.4
Calcium as single supplement (including antacids)												
No	64	85.3	129	78.7	1474	91.2	564	86.1	6379	78.9	8737	81.4
Yes	11	14.7	35	21.3	143	8.8	91	13.9	1703	21.1	2002	18.6
Single supplement (not Vitamin C, E, or calcium)												
No	48	64.0	103	62.8	1263	78.1	499	76.2	5541	68.6	7555	70.4
Yes	27	36.0	61	37.2	354	21.9	156	23.8	2541	31.4	3184	29.6
Any supplement (excluding single supplement calcium)												
No	32	42.7	65	39.6	940	58.1	368	56.2	3448	42.7	4914	45.8
Yes	43	57.3	99	60.4	677	41.9	287	43.8	4634	57.3	5825	54.2

[a]Total includes those of unknown ethnicity.
*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 3. Baseline demographic and general health characteristics of WHI Dietary Modification participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 203)			Asian/Pacific Islander (*N* = 1107)			Black (*N* = 5266)			Hispanic (*N* = 1854)			White (*N* = 39,760)			Total[a] (*N* = 48,836)		
Characteristic	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Age at screening (y)	203		61.0 ± 6.6	1107		61.0 ± 7.1	5266		60.8 ± 6.8	1854		59.7 ± 6.3	39,760		62.6 ± 6.8	48,836		62.3 ± 6.9
50–59	89	43.8		496	44.8		2386	45.3		972	52.4		13,806	34.7		18,003	36.9	
60–69	91	44.8		461	41.6		2267	43.0		739	39.9		18,877	47.5		22,713	46.5	
70– 79	23	11.3		150	13.6		613	11.6		143	7.7		7077	17.8		8120	16.6	
Education																		
0–8 y	*	*		*	*		100	1.9		258	14.2		200	0.5		576	1.2	
Some high school	13	6.5		24	2.2		367	7.0		163	8.9		1039	2.6		1639	3.4	
High school diploma/GED	35	17.6		165	15.1		699	13.4		311	17.1		7186	18.2		8518	17.6	
School after high school	105	52.8		381	34.8		2146	41.2		683	37.5		15,719	39.7		19,308	39.8	
College degree or higher	44	22.1		520	47.4		1901	36.5		407	22.3		15,412	39.0		18,488	38.1	
Family income																		
<$10,000	19	9.7		25	2.4		499	10.1		263	15.5		951	2.5		1783	3.9	
$10,000–$19,999	35	17.9		68	6.4		808	16.4		308	18.2		3982	10.6		5294	11.5	
$20,000–$34,999	47	24.1		160	15.2		1224	24.9		435	25.7		9298	24.8		11,315	24.6	
$35,000–$49,999	43	22.1		197	18.7		944	19.2		295	17.4		8220	21.9		9822	21.3	
$50,000–$74,999	37	19.0		308	29.2		892	18.1		251	14.8		7959	21.2		9549	20.8	
$75,000+	14	7.2		297	28.2		558	11.3		140	8.3		7133	19.0		8242	17.9	
Occupation																		
Managerial/Professional	66	36.9		488	46.0		2013	43.7		450	28.4		14,570	42.6		17,790	42.1	
Technical/Sales/ Administrative	50	27.9		373	35.2		1178	25.5		452	28.5		11,152	32.6		13,404	31.8	
Service/Labor	51	28.5		146	13.8		1106	24.0		394	24.8		5248	15.4		7079	16.8	
Homemaker only	12	6.7		53	5.0		314	6.8		290	18.3		3211	9.4		3934	9.3	
Body mass index (BMI), kg/m^2	202		30.4 ± 5.9	1103		26.1 ± 4.9	5234		32.1 ± 6.5	1842		29.8 ± 5.7	39,587		28.8 ± 5.7	48,612		29.1 ± 5.9
Underweight (<18.5)	0	0.0		19	1.7		12	0.2		*	*		118	0.3		154	0.3	
Normal (18.5–24.9)	41	20.3		500	45.3		600	11.5		353	19.2		10,872	27.5		12,503	25.7	
Overweight (25.0–29.9)	59	29.2		399	36.2		1579	30.2		681	37.0		14,456	36.5		17,387	35.8	
Obesity I (30.0–34.9)	58	28.7		131	11.9		1545	29.5		489	26.5		8794	22.2		11,198	23.0	
Obesity II (35.0–39.9)	28	13.9		40	3.6		911	17.4		219	11.9		3781	9.6		5048	10.4	
Obesity III (≥40)	16	7.9		14	1.3		587	11.2		96	5.2		1566	4.0		2322	4.8	
Marital status																		
Never married	6	3.0		58	5.3		289	5.6		76	4.2		1512	3.8		1970	4.1	
Divorced/Separated	49	24.5		124	11.3		1581	30.4		399	21.9		5433	13.7		7704	15.8	
Widowed	29	14.5		127	11.5		1072	20.6		232	12.7		6093	15.4		7646	15.7	
Presently married/ Living as married	116	58.0		793	72.0		2264	43.5		1115	61.2		26,601	67.1		31,293	64.4	
Height (cm)	39,647		161.8 ± 6.0	5241		155.5 ± 5.8	1846		162.7 ± 6.5	203		157.4 ± 6.2	1103		162.5 ± 6.4	48,685		162.1 ± 6.5
Weight (kg)	39,724		79.5 ± 15.9	5263		63.4 ± 13.9	1853		85.2 ± 18.4	202		74.3 ± 15.6	1107		76.1 ± 16.0	48,795		76.7 ± 16.5
Waist/hip ratio (WHR)	39,639		0.85 ± 0.1	5249		0.82 ± 0.1	1844		0.82 ± 0.1	202		0.82 ± 0.1	1104		0.82 ± 0.1	48,682		0.82 ± 0.1
Waist (cm)	39,659		93.7 ± 15.8	5255		81.2 ± 11.1	1845		93.6 ± 13.7	202		88.7 ± 13.4	1104		88.6 ± 13.7	48,711		89.0 ± 13.8
Living alone																		
No	153	76.1		965	87.6		3776	72.8		1542	84.9		30,719	77.7		37,676	77.7	
Yes	48	23.9		137	12.4		1411	27.2		275	15.1		8817	22.3		10,809	22.3	
U.S. region																		
Northeast	34	16.7		45	4.1		917	17.4		177	9.5		10,108	25.4		11,417	23.4	
South	50	24.6		53	4.8		2533	48.1		905	48.8		9104	22.9		12,745	26.1	
Midwest	19	9.4		28	2.5		1228	23.3		70	3.8		8539	21.5		9962	20.4	
West	100	49.3		981	88.6		588	11.2		702	37.9		12,009	30.2		14,712	30.1	

Smoking												
Never smoked	88	44.7	771	70.0	2519	48.7	1160	63.4	20,064	51.0	24,948	51.7
Past smoker	94	47.7	292	26.5	2086	40.3	546	29.9	16,839	42.8	20,101	41.6
Current smoker	15	7.6	39	3.5	566	10.9	123	6.7	2457	6.2	3250	6.7
Alcohol intake												
Never drinker	17	8.4	333	30.2	778	15.0	289	15.8	3269	8.3	4763	9.8
Past drinker	57	28.2	250	22.7	1707	32.8	412	22.5	6358	16.1	8900	18.4
<1 drink per mo	22	10.9	184	16.7	735	14.1	259	14.2	5302	13.4	6604	13.6
<1 drink per wk	44	21.8	195	17.7	1034	19.9	433	23.7	8804	22.3	10,657	22.0
1–<7 drinks per wk	46	22.8	113	10.3	744	14.3	353	19.3	11,507	29.1	12,914	26.6
7+ drinks per wk	16	7.9	27	2.5	205	3.9	82	4.5	4271	10.8	4650	9.6
Physical activity												
No activity	46	24.3	204	18.9	1301	26.5	425	25.2	6519	18.5	8621	19.7
Some activity	82	43.4	476	44.1	2267	46.1	760	45.1	15,331	43.4	19,164	43.8
2–<4 episodes per wk of moderate + activity	26	13.8	206	19.1	673	13.7	229	13.6	6270	17.8	7523	17.2
4+ episodes per wk of moderate + activity	35	18.5	194	18.0	673	13.7	272	16.1	7171	20.3	8454	19.3
Total expenditure/wk from physical activity (METs)												
0–1.5	62	32.8	275	25.5	1717	34.9	580	34.4	9155	25.9	11,958	27.3
>1.5–8	45	23.8	297	27.5	1541	31.4	489	29.0	10,379	29.4	12,920	29.5
>8–19	51	27.0	292	27.0	1038	21.1	374	22.2	9493	26.9	11,405	26.1
>19	31	16.4	216	20.0	618	12.6	243	14.4	6264	17.7	7479	17.1
Total calcium intake (mg)												
0–<400	28	13.8	182	16.5	1326	25.3	243	13.2	2649	6.7	4531	9.3
400–<800	58	28.6	324	29.4	2109	40.2	584	31.7	11,408	28.8	14,667	30.2
800–<1000	35	17.2	144	13.1	589	11.2	246	13.3	5662	14.3	6753	13.9
1000–<1200	22	10.8	143	13.0	375	7.1	207	11.2	4785	12.1	5604	11.5
1200+	60	29.6	310	28.1	846	16.1	564	30.6	15,071	38.1	17,059	35.1
Any supplement use												
No	76	37.4	325	29.4	2674	50.8	842	45.4	13,109	33.0	17,266	35.4
Yes	127	62.6	782	70.6	2592	49.2	1012	54.6	26,651	67.0	31,570	64.6
Multivitamin use (with or without minerals)												
No	135	66.5	732	66.1	4070	77.3	1371	73.9	24,756	62.3	31,497	64.5
Yes	68	33.5	375	33.9	1196	22.7	483	26.1	15,003	37.7	17,338	35.5
Vitamin C as single supplement												
No	158	77.8	819	74.0	4433	84.2	1512	81.6	30,084	75.7	37,503	76.8
Yes	45	22.2	288	26.0	833	15.8	342	18.4	9676	24.3	11,333	23.2
Vitamin E as single supplement												
No	158	77.8	784	70.8	4447	84.4	1468	79.2	29,099	73.2	36,447	74.6
Yes	45	22.2	323	29.2	819	15.6	386	20.8	10,661	26.8	12,389	25.4
Calcium as single supplement (including antacids)												
No	160	78.8	803	72.5	4672	88.7	1516	81.8	29,412	74.0	37,074	75.9
Yes	43	21.2	304	27.5	594	11.3	338	18.2	10,348	26.0	11,762	24.1
Single supplement (not Vitamin C, E, or calcium)												
No	135	66.5	666	60.2	4002	76.0	1319	71.1	25,658	64.5	32,198	65.9
Yes	68	33.5	441	39.8	1264	24.0	535	28.9	14,102	35.5	16,638	34.1
Any supplement (excluding single supplement calcium)												
No	85	41.9	383	34.6	2883	54.7	918	49.5	15,023	37.8	19,558	40.0
Yes	118	58.1	724	65.4	2383	45.3	936	50.5	24,737	62.2	29,278	60.0

[a]Total includes those of unknown ethnicity.
*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 4. Baseline demographic and general health characteristics of WHI Calcium and Vitamin D participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 149)			Asian/Pacific Islander (*N* = 722)			Black (*N* = 3317)			Hispanic (*N* = 1507)			White (*N* = 30,153)			Total[a] (*N* = 36,282)		
Characteristic	*N*	%	Mean ± SD	*N*	%	Mean ± SD	N	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Age at screening (y)	149		61.5 ± 6.7	722		61.4 ± 7.1	3317		60.6 ± 6.8	1507		59.3 ± 6.4	30,153		62.7 ± 6.9	36,282		62.4 ± 7.0
50–59	61	40.9		309	42.8		1572	47.4		844	56.0		10,469	34.7		13,422	37.0	
60–69	68	45.6		301	41.7		1354	40.8		546	36.2		14,057	46.6		16,520	45.5	
70–79	20	13.4		112	15.5		391	11.8		117	7.8		5627	18.7		6340	17.5	
Education																		
0–8 y	*	*		*	*		67	2.0		259	17.4		175	0.6		527	1.5	
Some high school	10	6.8		23	3.2		280	8.5		143	9.6		895	3.0		1375	3.8	
High school diploma/GED	26	17.6		105	14.7		476	14.5		273	18.4		5713	19.1		6673	18.5	
School after high school	72	48.6		267	37.3		1389	42.4		538	36.2		11,921	39.8		14,372	39.9	
College degree or higher	37	25.0		315	44.1		1064	32.5		272	18.3		11,285	37.6		13,098	36.3	
Family income																		
<$10,000	11	7.6		24	3.5		330	10.6		281	20.5		790	2.8		1465	4.3	
$10,000–$19,999	30	20.7		63	9.1		553	17.7		273	19.9		3365	11.7		4353	12.6	
$20,000–$34,999	33	22.8		120	17.4		798	25.6		320	23.3		7544	26.3		8911	25.9	
$35,000–$49,999	29	20.0		133	19.2		586	18.8		215	15.7		6250	21.8		7302	21.2	
$50,000–$74,999	30	20.7		178	25.8		526	16.9		180	13.1		5866	20.4		6849	19.9	
$75,000+	12	8.3		173	25.0		326	10.5		102	7.4		4876	17.0		5546	16.1	
Occupation																		
Managerial/Professional	52	38.8		300	43.4		1162	40.4		327	24.9		10,837	41.1		12,813	40.3	
Technical/Sales/ Administrative	35	26.1		234	33.9		770	26.8		367	27.9		8573	32.5		10,102	31.8	
Service/Labor	40	29.9		118	17.1		723	25.1		356	27.1		4485	17.0		5815	18.3	
Homemaker only	7	5.2		39	5.6		220	7.7		265	20.2		2495	9.5		3069	9.7	
Body mass index (BMI), kg/m^2	149		30.8 ± 6.0	720		26.0 ± 4.8	3296		31.9 ± 6.7	1495		29.8 ± 5.6	30,002		28.7 ± 5.8	36,095		29.0 ± 5.9
Underweight (<18.5)	0	0.0		11	1.5		7	0.2		*	*		126	0.4		148	0.4	
Normal (18.5–24.9)	25	16.8		335	46.5		415	12.6		279	18.7		8278	27.6		9430	26.1	
Overweight (25.0–29.9)	47	31.5		248	34.4		1030	31.3		580	38.8		10,907	36.4		12,955	35.9	
Obesity I (30.0–34.9)	42	28.2		89	12.4		926	28.1		392	26.2		6639	22.1		8203	22.7	
Obesity II (35.0–39.9)	22	14.8		32	4.4		543	16.5		161	10.8		2834	9.4		3644	10.1	
Obesity III (≥40)	13	8.7		5	0.7		375	11.4		79	5.3		1218	4.1		1715	4.8	
Marital status																		
Never married	*	*		39	5.4		194	5.9		62	4.2		1120	3.7		1437	4.0	
Divorced/Separated	40	26.8		102	14.2		1014	30.9		327	22.0		4158	13.8		5724	15.8	
Widowed	22	14.8		92	12.8		684	20.9		203	13.6		4939	16.4		6012	16.6	
Presently married/ Living as married	85	57.0		484	67.5		1387	42.3		896	60.2		19,853	66.0		22,962	63.5	
Height (cm)	149		161.7 ± 6.1	720		155.2 ± 5.8	3301		162.6 ± 6.4	1498		157.3 ± 6.3	30,062		162.4 ± 6.3	36,163		162.0 ± 6.5
Weight (kg)	149		80.6 ± 16.2	722		63.0 ± 13.5	3314		84.5 ± 18.4	1507		74.2 ± 15.9	30,112		76.0 ± 16.1	36,238		76.4 ± 16.6
Waist/hip ratio (WHR)	147		0.83 ± 0.1	720		0.82 ± 0.1	3301		0.83 ± 0.1	1500		0.82 ± 0.1	30,048		0.82 ± 0.1	36,149		0.82 ± 0.1
Waist (cm)	147		92.8 ± 13.8	720		81.1 ± 11.0	3307		93.2 ± 13.6	1501		88.7 ± 13.2	30,070		88.5 ± 13.7	36,179		88.9 ± 13.7
Living alone																		
No	121	82.9		613	85.1		2391	73.1		1249	84.6		23,226	77.4		27,952	77.6	
Yes	25	17.1		107	14.9		881	26.9		227	15.4		6766	22.6		8085	22.4	
U.S. region																		
Northeast	27	18.1		30	4.2		537	16.2		161	10.7		7189	23.8		8019	22.1	
South	39	26.2		42	5.8		1545	46.6		720	47.8		6219	20.6		8631	23.8	
Midwest	16	10.7		30	4.2		921	27.8		58	3.8		7750	25.7		8828	24.3	
West	67	45.0		620	85.9		314	9.5		568	37.7		8995	29.8		10,804	29.8	

Smoking												
Never smoked	68	46.9	500	69.5	1592	48.9	943	63.4	15,424	51.6	18,753	52.2
Past smoker	62	42.8	181	25.2	1275	39.1	443	29.8	12,262	41.1	14,388	40.1
Current smoker	15	10.3	38	5.3	391	12.0	101	6.8	2180	7.3	2761	7.7
Alcohol intake												
Never drinker	17	11.4	235	32.6	513	15.6	282	19.1	2649	8.8	3754	10.4
Past drinker	41	27.5	148	20.6	1039	31.7	337	22.8	4748	15.8	6401	17.8
<1 drink per mo	18	12.1	119	16.5	453	13.8	226	15.3	4165	13.9	5049	14.0
<1 drink per wk	29	19.5	125	17.4	659	20.1	299	20.2	6417	21.4	7621	21.2
1–<7 drinks per wk	30	20.1	75	10.4	492	15.0	271	18.3	8435	28.1	9389	26.1
7+ drinks per wk	14	9.4	18	2.5	122	3.7	65	4.4	3556	11.9	3810	10.6
Physical activity												
No activity	28	20.3	126	17.8	792	25.5	343	24.7	4938	18.1	6324	19.2
Some activity	69	50.0	319	45.0	1420	45.7	651	46.8	11,691	42.9	14,312	43.4
2–<4 episodes per wk of moderate + activity	18	13.0	132	18.6	447	14.4	173	12.4	4694	17.2	5534	16.8
4+ episodes per wk of moderate + activity	23	16.7	132	18.6	451	14.5	223	16.0	5920	21.7	6824	20.7
Total expenditure/wk from physical activity (METs)												
0–1.5	41	29.7	176	24.8	1050	33.8	463	33.3	6855	25.2	8709	26.4
>1.5–8	43	31.2	182	25.7	956	30.7	402	28.9	7902	29.0	9589	29.1
>8–19	35	25.4	205	28.9	667	21.4	322	23.2	7283	26.7	8609	26.1
>19	19	13.8	146	20.6	437	14.1	203	14.6	5203	19.1	6087	18.4
Total calcium intake (mg)												
0–<400	20	14.0	121	17.2	794	24.9	205	14.3	2033	6.8	3248	9.1
400–<800	34	23.8	224	31.8	1254	39.3	453	31.5	8552	28.8	10,635	29.9
800–<1000	36	25.2	85	12.1	365	11.4	192	13.4	4302	14.5	5030	14.1
1000–<1200	18	12.6	86	12.2	238	7.5	162	11.3	3617	12.2	4170	11.7
1200+	35	24.5	188	26.7	539	16.9	424	29.5	11,189	37.7	12,500	35.1
Any supplement use												
No	54	36.2	212	29.4	1666	50.2	696	46.2	10,090	33.5	12,878	35.5
Yes	95	63.8	510	70.6	1651	49.8	811	53.8	20,063	66.5	23,404	64.5
Multivitamin use (with or without minerals)												
No	99	66.4	482	66.8	2571	77.5	1122	74.5	18,791	62.3	23,354	64.4
Yes	50	33.6	240	33.2	745	22.5	385	25.5	11,362	37.7	12,927	35.6
Vitamin C as single supplement												
No	115	77.2	536	74.2	2818	85.0	1255	83.3	23,034	76.4	28,094	77.4
Yes	34	22.8	186	25.8	499	15.0	252	16.7	7119	23.6	8188	22.6
Vitamin E as single supplement												
No	114	76.5	501	69.4	2783	83.9	1195	79.3	22,297	73.9	27,224	75.0
Yes	35	23.5	221	30.6	534	16.1	312	20.7	7856	26.1	9058	25.0
Calcium as single supplement (including antacids)												
No	124	83.2	534	74.0	2911	87.8	1263	83.8	22,442	74.4	27,626	76.1
Yes	25	16.8	188	26.0	406	12.2	244	16.2	7711	25.6	8656	23.9
Single supplement (not Vitamin C, E, or calcium)												
No	96	64.4	435	60.2	2501	75.4	1073	71.2	19,756	65.5	24,147	66.6
Yes	53	35.6	287	39.8	816	24.6	434	28.8	10,397	34.5	12,135	33.4
Any supplement (excluding single supplement calcium)												
No	60	40.3	249	34.5	1809	54.5	754	50.0	11,551	38.3	14,600	40.2
Yes	89	59.7	473	65.5	1508	45.5	753	50.0	18,602	61.7	21,682	59.8

[a]Total includes those of unknown ethnicity.
*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 5. Baseline demographic and general health characteristics of WHI Observational Study participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 422)			Asian/Pacific Islander (*N* = 2671)			Black (*N* = 7639)			Hispanic (*N* = 3623)			White (*N* = 78,013)			Total[a] (*N* = 93,676)		
Characteristic	*N*	%	Mean ± SD	*N*	%	Mean ± D	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Age at screening (y)	422		61.7 ± 7.9	2671		63.8 ± 7.6	7639		62.1 ± 7.3	3623		60.6 ± 7.1	78,013		63.9 ± 7.3	93,676		63.6 ± 7.4
50–59	178	42.2		861	32.2		2978	39.0		1761	48.6		23,565	30.2		29,705	31.7	
60–69	161	38.2		1102	41.3		3256	42.6		1399	38.6		34,677	44.5		41,197	44.0	
70–79	83	19.7		708	26.5		1405	18.4		463	12.8		19,771	25.3		22,774	24.3	
Education																		
0–8 y	46	11.0		65	2.5		277	3.7		630	17.7		518	0.7		1560	1.7	
Some high school	46	11.0		95	3.6		726	9.6		318	8.9		2032	2.6		3288	3.5	
High school diploma/GED	69	16.5		416	15.7		1047	13.9		564	15.9		12,784	16.5		15,121	16.3	
School after high school	166	39.7		891	33.6		2789	37.0		1249	35.1		28,332	36.6		33,933	36.5	
College degree or higher	91	21.8		1185	44.7		2692	35.7		796	22.4		33,781	43.6		39,002	42.0	
Family income																		
<$10,000	67	17.6		84	3.4		967	13.9		544	17.1		2175	3.0		3916	4.5	
$10,000–$19,999	78	20.5		241	9.7		1252	18.0		639	20.1		7704	10.6		10,100	11.6	
$20,000–$34,999	96	25.2		498	20.1		1635	23.5		745	23.4		16,953	23.4		20,226	23.3	
$35,000–$49,999	55	14.4		464	18.7		1228	17.6		531	16.7		14,932	20.6		17,429	20.1	
$50,000–$74,999	51	13.4		555	22.4		1149	16.5		409	12.9		15,092	20.8		17,486	20.2	
$75,000+	34	8.9		637	25.7		732	10.5		311	9.8		15,713	21.7		17,608	20.3	
Occupation																		
Managerial/Professional	119	30.2		1094	42.1		2908	41.4		863	25.9		33,176	44.5		38,622	43.3	
Technical/Sales/ Administrative	98	24.9		835	32.1		1729	24.6		858	25.7		21,583	28.9		25,480	28.6	
Service/Labor	119	30.2		480	18.5		1809	25.8		906	27.2		11,847	15.9		15,470	17.3	
Homemaker only	58	14.7		191	7.3		575	8.2		706	21.2		8030	10.8		9658	10.8	
Body mass index (BMI), kg/m^2	409		29.7 ± 6.8	2654		24.2 ± 4.3	7539		30.7 ± 6.8	3570		28.6 ± 5.9	77,107		27.0 ± 5.7	92,568		27.3 ± 5.9
Underweight (<18.5)	5	1.2		119	4.5		52	0.7		15	0.4		903	1.2		1107	1.2	
Normal (18.5–24.9)	112	27.4		1565	59.0		1394	18.5		1012	28.3		32,134	41.7		36,687	39.6	
Overweight (25.0–29.9)	116	28.4		758	28.6		2551	33.8		1366	38.3		26,202	34.0		31,463	34.0	
Obesity I (30.0–34.9)	100	24.4		154	5.8		1899	25.2		751	21.0		11,466	14.9		14,578	15.7	
Obesity II (35.0–39.9)	44	10.8		36	1.4		928	12.3		283	7.9		4080	5.3		5451	5.9	
Obesity III (≥40)	32	7.8		22	0.8		715	9.5		143	4.0		2322	3.0		3282	3.5	
Height (cm)	412		160.4 ± 7.3	2657		154.8 ± 6.0	7575		162.3 ± 6.8	3576		157.2 ± 6.2	77,406		162.1 ± 6.6	92,920		161.7 ± 6.8
Weight (kg)	420		78.0 ± 20.8	2666		58.3 ± 12.2	7603		81.4 ± 19.3	3610		71.2 ± 16.6	77,605		71.2 ± 16.3	93,204		71.7 ± 16.9
Waist/hip ratio (WHR)	421		0.84 ± 0.1	2662		0.81 ± 0.1	7607		0.82 ± 0.1	3610		0.82 ± 0.1	77,568		0.80 ± 0.1	93,167		0.81 ± 0.1
Waist (cm)	421		91.8 ± 15.7	2666		77.4 ± 10.3	7618		90.8 ± 14.4	3613		85.9 ± 12.7	77,659		84.4 ± 13.5	93,279		84.8 ± 13.7
Marital status																		
Never married	19	4.6		157	5.9		493	6.5		180	5.0		3473	4.5		4390	4.7	
Divorced/Separated	86	20.7		302	11.4		2279	30.1		799	22.4		11,024	14.2		14,727	15.8	
Widowed	87	20.9		422	15.9		1803	23.8		541	15.1		13,174	17.0		16,290	17.5	
Presently married/ Living as married	224	53.8		1776	66.8		2990	39.5		2051	57.4		50,034	64.4		57,805	62.0	
Living alone																		
No	310	74.0		2192	82.6		5012	66.7		2800	79.6		57,086	73.6		68,310	73.5	
Yes	109	26.0		461	17.4		2499	33.3		717	20.4		20,436	26.4		24,603	26.5	
U.S. region																		
Northeast	49	11.6		138	5.2		1292	16.9		460	12.7		19,067	24.4		21,273	22.7	
South	94	22.3		172	6.4		3543	46.4		1360	37.5		19,028	24.4		24,459	26.1	
Midwest	39	9.2		112	4.2		1897	24.8		138	3.8		18,219	23.4		20,607	22.0	
West	240	56.9		2249	84.2		907	11.9		1665	46.0		21,699	27.8		27,337	29.2	

Years lived in current state												
<5	20	4.8	58	2.2	240	3.2	156	4.4	2804	3.6	3322	3.6
5–9	19	4.6	76	2.9	231	3.1	170	4.8	3035	3.9	3584	3.9
10–19	33	8.0	242	9.1	455	6.0	360	10.3	6219	8.0	7440	8.0
20+	343	82.7	2283	85.9	6612	87.7	2825	80.5	65,550	84.5	78,680	84.6
Born in the U.S.												
No	14	3.4	723	27.2	243	3.2	1313	37.3	4234	5.5	6802	7.3
Yes	401	96.6	1938	72.8	7267	96.8	2205	62.7	73,450	94.5	86,281	92.7
U.S. region of birth												
Not born in U.S.	14	3.4	723	27.2	243	3.3	1313	40.9	4234	5.5	6802	7.4
Northeast	59	14.4	33	1.2	864	11.6	158	4.9	24,326	31.4	25,763	27.9
South	137	33.3	22	0.8	5135	68.8	861	26.8	13,994	18.1	20,318	22.0
Midwest	62	15.1	43	1.6	1060	14.2	84	2.6	25,598	33.1	27,077	29.3
West	139	33.8	1834	69.1	160	2.1	798	24.8	9273	12.0	12,498	13.5
Smoking												
Never smoked	210	51.0	1963	74.0	3735	50.0	2236	63.4	38,169	49.6	47,023	50.9
Past smoker	157	38.1	599	22.6	2902	38.9	1055	29.9	34,305	44.6	39,514	42.8
Current smoker	45	10.9	92	3.5	828	11.1	237	6.7	4513	5.9	5791	6.3
Years as a child lived with smoker												
Never lived with a smoker	126	31.4	1008	39.4	3153	43.0	1437	42.3	26,892	35.2	33,137	36.2
<1	8	2.0	34	1.3	141	1.9	62	1.8	555	0.7	819	0.9
1–4	13	3.2	76	3.0	273	3.7	108	3.2	2093	2.7	2602	2.8
5–9	33	8.2	178	7.0	510	7.0	227	6.7	4217	5.5	5246	5.7
10–18	221	55.1	1263	49.4	3249	44.3	1566	46.1	42,729	55.9	49,636	54.3
Years as adult lived with smoker												
Never lived with a smoker	98	23.9	964	36.3	1745	23.3	1270	36.4	19,903	25.8	24,362	26.3
<1	10	2.4	71	2.7	227	3.0	99	2.8	1566	2.0	2012	2.2
1–4	34	8.3	276	10.4	704	9.4	281	8.1	7751	10.0	9155	9.9
5–9	29	7.1	268	10.1	797	10.7	288	8.3	7094	9.2	8573	9.3
10–19	68	16.6	368	13.8	1329	17.8	506	14.5	12,164	15.8	14,650	15.8
20–29	68	16.6	318	12.0	1097	14.7	447	12.8	11,781	15.3	13,888	15.0
30–39	59	14.4	228	8.6	793	10.6	324	9.3	9221	11.9	10,768	11.6
40+	44	10.7	165	6.2	784	10.5	274	7.9	7741	10.0	9133	9.9
Years worked with smoker												
Never worked with a smoker	129	31.2	792	29.9	1490	20.0	1266	36.2	19,350	25.1	23,343	25.3
<1	15	3.6	101	3.8	242	3.2	183	5.2	2792	3.6	3377	3.7
1–4	57	13.8	400	15.1	806	10.8	522	14.9	12,542	16.3	14,517	15.7
5–9	55	13.3	339	12.8	973	13.0	493	14.1	12,254	15.9	14,304	15.5
10–19	71	17.2	435	16.4	1591	21.3	529	15.1	14,554	18.9	17,408	18.8
20–29	52	12.6	357	13.5	1451	19.5	321	9.2	9365	12.1	11,722	12.7
30–39	21	5.1	157	5.9	659	8.8	122	3.5	4186	5.4	5241	5.7
40+	13	3.1	72	2.7	245	3.3	59	1.7	2094	2.7	2526	2.7
Alcohol intake												
Never drinker	80	19.2	1081	40.6	1419	18.9	725	20.4	6969	9.0	10,477	11.3
Past drinker	120	28.8	528	19.8	2557	34.0	856	24.1	13,202	17.0	17,555	18.9
<1 drink per mo	42	10.1	353	13.3	938	12.5	440	12.4	8799	11.3	10,733	11.5
<1 drink per wk	72	17.3	373	14.0	1275	17.0	721	20.3	16,023	20.6	18,728	20.1
1–<7 drinks per wk	74	17.7	244	9.2	987	13.1	629	17.7	21,654	27.9	23,842	25.6
7+ drinks per wk	29	7.0	82	3.1	340	4.5	177	5.0	10,962	14.1	11,709	12.6
Physical activity												
No activity	80	19.2	351	13.2	1614	21.3	695	19.9	9709	12.6	12,637	13.6
Some activity	188	45.1	1170	44.1	3309	43.7	1563	44.8	28,879	37.4	35,648	38.5
2–<4 episodes per wk of moderate + activity	52	12.5	448	16.9	1183	15.6	498	14.3	14,685	19.0	17,093	18.5
4+ episodes per wk of moderate + activity	97	23.3	684	25.8	1460	19.3	732	21.0	23,936	31.0	27,251	29.4

(*continued*)

APPENDIX TABLE 5. *Continued*

	Race/Ethnicity																	
	American Indian (*N* = 422)			Asian/Pacific Islander (*N* = 2671)			Black (*N* = 7639)			Hispanic (*N* = 3623)			White (*N* = 78,013)			Total[a] (*N* = 93,676)		
Characteristic	*N*	%	Mean ± SD	*N*	%	Mean ± D	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Total expenditure/wk from physical activity (METs)																		
0–1.5	121	29.0		506	19.1		2202	29.1		939	26.9		13,853	17.9		17,888	19.3	
>1.5–8	107	25.7		670	25.3		2164	28.6		1017	29.2		19,027	24.6		23,330	25.2	
>8–19	89	21.3		764	28.8		1825	24.1		831	23.8		23,335	30.2		27,205	29.4	
>19	100	24.0		713	26.9		1375	18.2		701	20.1		20,994	27.2		24,206	26.1	
Total calcium intake (mg)																		
0–<400	52	13.6		410	16.4		1732	25.7		459	14.1		4630	6.1		7423	8.3	
400–<800	113	29.6		678	27.2		2515	37.3		987	30.3		18,425	24.3		23,076	25.7	
800–<1000	58	15.2		316	12.7		766	11.3		456	14.0		9531	12.6		11,267	12.5	
1000–<1200	35	9.2		271	10.9		551	8.2		327	10.0		9194	12.1		10,505	11.7	
1200+	124	32.5		822	32.9		1185	17.6		1025	31.5		34,024	44.9		37,645	41.9	
Any supplement use																		
No	183	43.4		650	24.3		3522	46.1		1452	40.1		19,373	24.8		25,567	27.3	
Yes	239	56.6		2021	75.7		4117	53.9		2171	59.9		58,640	75.2		68,109	72.7	
Multivitamin use (with or without minerals)																		
No	304	72.0		1684	63.0		5593	73.2		2594	71.6		43,842	56.2		54,840	58.5	
Yes	118	28.0		987	37.0		2046	26.8		1029	28.4		34,171	43.8		38,836	41.5	
Vitamin C as single supplement																		
No	337	79.9		1814	67.9		6283	82.2		2923	80.7		54,312	69.6		66,594	71.1	
Yes	85	20.1		857	32.1		1356	17.8		700	19.3		23,701	30.4		27,082	28.9	
Vitamin E as single supplement																		
No	316	74.9		1700	63.6		6141	80.4		2828	78.1		50,453	64.7		62,332	66.5	
Yes	106	25.1		971	36.4		1498	19.6		795	21.9		27,560	35.3		31,344	33.5	
Calcium as single supplement (including antacids)																		
No	339	80.3		1869	70.0		6591	86.3		2828	78.1		54,391	69.7		66,990	71.5	
Yes	83	19.7		802	30.0		1048	13.7		795	21.9		23,622	30.3		26,686	28.5	
Single supplement (not Vitamin C, E, or calcium)																		
No	286	67.8		1470	55.0		5607	73.4		2468	68.1		44,110	56.5		54,698	58.4	
Yes	136	32.2		1201	45.0		2032	26.6		1155	31.9		33,903	43.5		38,978	41.6	
Any supplement (excluding single supplement calcium)																		
No	198	46.9		773	28.9		3731	48.8		1613	44.5		22,100	28.3		28,844	30.8	
Yes	224	53.1		1898	71.1		3908	51.2		2010	55.5		55,913	71.7		64,832	69.2	

[a]Total includes those of unknown ethnicity.
*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 6. Baseline medical history of WHI Estrogen + Progestin participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 56)			Asian/Pacific Islander (*N* = 363)			Black (*N* = 1124)			Hispanic (*N* = 888)			White (*N* = 13,945)			Total[a] (*N* = 16,608)		
Medical History	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Age at menopause (y)																		
<40	*	*		6	1.7		47	4.6		26	3.4		297	2.3		384	2.5	
40–49	16	33.3		117	33.3		371	36.3		331	43.2		4356	33.8		5271	34.5	
50+	31	64.6		228	65.0		604	59.1		410	53.5		8216	63.8		9617	63.0	
Bilateral oophorectomy																		
No	55	98.2		361	100.0		1108	99.6		872	99.7		13,849	99.7		16,474	99.7	
Yes	*	*		0	0.0		*	*		*	*		43	0.3		53	0.3	
Ever pregnant																		
No	*	*		36	9.9		62	5.6		58	6.6		1110	8.0		1288	7.8	
Yes	53	94.6		327	90.1		1054	94.4		825	93.4		12,819	92.0		15,291	92.2	
Age at first birth (y)[b]																		
Never had term pregnancy	0	0.0		5	1.8		60	6.9		19	3.1		312	2.7		400	2.9	
<20	18	39.1		16	5.8		280	32.1		173	28.3		1708	14.6		2236	16.4	
20–29	23	50.0		209	76.0		462	53.0		355	58.0		8513	72.9		9670	70.8	
30+	5	10.9		45	16.4		69	7.9		65	10.6		1142	9.8		1344	9.8	
Number of live births																		
Never pregnant	*	*		36	9.9		62	5.6		58	6.6		1110	8.0		1288	7.8	
None	0	0.0		*	*		65	5.8		21	2.4		327	2.4		422	2.6	
1	*	*		38	10.5		164	14.7		79	9.0		1078	7.8		1389	8.4	
2–4	27	48.2		235	64.9		599	53.9		507	57.8		8994	64.7		10,503	63.5	
5+	19	33.9		48	13.3		222	20.0		212	24.2		2383	17.2		2928	17.7	
Number of pregnancies																		
Never pregnant	*	*		36	9.9		62	5.6		58	6.6		1110	8.0		1288	7.8	
1	*	*		26	7.2		91	8.2		48	5.4		882	6.3		1070	6.5	
2–4	26	46.4		76	20.9		396	35.7		346	39.3		3859	27.8		4781	28.9	
5+	23	41.1		225	62.0		559	50.5		429	48.7		8052	57.9		9403	56.8	
Any induced abortions[b]																		
Pregnant, never had abortion	44	91.7		273	88.1		746	78.9		608	85.6		11,030	92.5		12,879	91.1	
One or more abortions	*	*		37	11.9		200	21.1		102	14.4		894	7.5		1258	8.9	
Number of months breastfed																		
Never breastfed	27	48.2		116	32.4		535	48.6		355	40.9		6354	46.0		7482	45.6	
1–6	14	25.0		104	29.1		324	29.4		236	27.2		3492	25.3		4239	25.8	
7–12	5	8.9		64	17.9		125	11.4		107	12.3		1552	11.2		1882	11.5	
13–23	*	*		41	11.5		59	5.4		81	9.3		1422	10.3		1627	9.9	
24+	8	14.3		33	9.2		58	5.3		89	10.3		982	7.1		1185	7.2	
Age at tubal ligation (y)																		
Never had tubal ligation	34	63.0		267	74.2		778	70.5		635	72.2		11,311	81.4		13,207	80.0	
<30	*	*		11	3.1		43	3.9		38	4.3		326	2.3		426	2.6	
30–34	*	*		25	6.9		88	8.0		59	6.7		650	4.7		843	5.1	
35–39	*	*		43	11.9		127	11.5		90	10.2		908	6.5		1190	7.2	
40–44	*	*		11	3.1		58	5.3		51	5.8		561	4.0		694	4.2	
45+	0	0.0		*	*		10	0.9		*	*		133	1.0		157	1.0	

(*continued*)

APPENDIX TABLE 6. *Continued*

Age last had any menstrual bleeding (y)												
<40	*	*	*	*	36	3.6	22	3.0	180	1.5	246	1.7
40–44	7	14.6	23	6.7	78	7.9	76	10.4	862	7.0	1071	7.3
45–49	8	16.7	86	25.1	260	26.3	210	28.7	2893	23.5	3497	23.9
50–54	27	56.3	171	50.0	422	42.7	335	45.8	6008	48.8	7049	48.2
55–59	6	12.5	50	14.6	165	16.7	75	10.2	1979	16.1	2319	15.9
60+	*	*	8	2.3	28	2.8	14	1.9	385	3.1	442	3.0
Current health care provider												
No	9	16.1	34	9.4	151	13.8	280	32.2	1432	10.4	1935	11.8
Yes	47	83.9	327	90.6	947	86.2	590	67.8	12,389	89.6	14,501	88.2
Mammogram in last 2 y												
No	18	34.6	107	30.0	271	25.6	345	42.1	3810	28.2	4624	28.9
Yes	34	65.4	250	70.0	786	74.4	475	57.9	9691	71.8	11,386	71.1
Pap smear in last 3 y												
No	11	22.4	69	20.5	146	16.1	215	29.8	2297	19.8	2781	20.1
Yes	38	77.6	267	79.5	759	83.9	506	70.2	9318	80.2	11,048	79.9
Total oral contraceptive duration (y)												
Non-user	34	60.7	225	62.0	648	57.7	523	58.9	7887	56.6	9466	57.0
<5	13	23.2	78	21.5	220	19.6	205	23.1	3198	22.9	3765	22.7
5–<10	*	*	31	8.5	108	9.6	86	9.7	1393	10.0	1634	9.8
10+	*	*	29	8.0	148	13.2	74	8.3	1467	10.5	1743	10.5
History of PHT use[c]												
Never	46	82.1	266	73.3	891	79.3	667	75.2	10,164	72.9	12,192	73.4
Past	8	14.3	51	14.0	172	15.3	150	16.9	2702	19.4	3135	18.9
Current	*	*	46	12.7	60	5.3	70	7.9	1073	7.7	1273	7.7
Total PHT duration (y)[c]												
Nonuser	46	82.1	266	73.3	891	79.3	667	75.1	10,164	72.9	12,192	73.4
<5	8	14.3	62	17.1	185	16.5	157	17.7	2657	19.1	3118	18.8
5–<9	0	0.0	26	7.2	34	3.0	46	5.2	663	4.8	783	4.7
10–<14	*	*	5	1.4	11	1.0	13	1.5	300	2.2	336	2.0
15+	*	*	*	*	*	*	5	0.6	160	1.1	178	1.1
History of E-alone use[c]												
Never	52	92.9	343	94.5	1024	91.2	816	92.0	12,323	88.4	14,756	88.9
Past	*	*	18	5.0	86	7.7	61	6.9	1510	10.8	1709	10.3
Current	*	*	*	*	13	1.2	10	1.1	107	0.8	136	0.8
Total E-alone duration (y)[c]												
Nonuser	52	92.9	343	94.5	1024	91.1	816	91.9	12,323	88.4	14,756	88.9
<5	*	*	15	4.1	78	6.9	56	6.3	1242	8.9	1416	8.5
5–<10	0	0.0	*	*	18	1.6	11	1.2	209	1.5	250	1.5
10–<15	0	0.0	*	*	*	*	5	0.6	107	0.8	117	0.7
15+	*	*	*	*	0	0.0	0	0.0	63	0.5	68	0.4

History of E + P use[c]																			
Never	49	87.5		278	76.6		977	86.9		730	82.2		11,402	81.8		13,620	82.0		
Past	6	10.7		41	11.3		99	8.8		98	11.0		1560	11.2		1833	11.0		
Current	*	*		44	12.1		48	4.3		60	6.8		979	7.0		1151	6.9		
Total E + P duration (y)[c]																			
Nonuser	49	87.5		278	76.6		977	86.9		730	82.2		11,402	81.8		13,620	82.0		
<5	6	10.7		57	15.7		121	10.8		111	12.5		1804	12.9		2133	12.8		
5–<10	0	0.0		21	5.8		17	1.5		34	3.8		487	3.5		568	3.4		
10–<15	*	*		*	*		8	0.7		9	1.0		182	1.3		207	1.2		
15+	0	0.0		*	*		*	*		*	*		70	0.5		80	0.5		
Family history of MI																			
No	24	47.1		207	61.1		587	58.1		484	58.4		6283	47.3		7687	48.9		
Yes	27	52.9		132	38.9		424	41.9		345	41.6		6992	52.7		8032	51.1		
Family history of breast cancer																			
No	37	78.7		307	89.2		920	88.0		766	90.4		11,043	83.5		13,256	84.3		
Yes	10	21.3		37	10.8		126	12.0		81	9.6		2176	16.5		2461	15.7		
Family history of colorectal cancer																			
No	36	83.7		293	87.2		826	85.1		722	89.9		10,757	84.0		12,814	84.5		
Yes	7	16.3		43	12.8		145	14.9		81	10.1		2046	16.0		2348	15.5		
Family history of stroke																			
No	28	58.3		194	56.2		600	57.4		565	69.1		8120	61.5		9620	61.4		
Yes	20	41.7		151	43.8		446	42.6		253	30.9		5081	38.5		6047	38.6		
Family history of adult diabetes																			
No	28	54.9		209	61.3		485	48.6		475	57.3		9159	68.6		10,488	66.5		
Yes	23	45.1		132	38.7		513	51.4		354	42.7		4190	31.4		5286	33.5		
Parent broke bone after age 40																			
No	32	74.4		235	69.7		758	79.8		566	69.7		7415	57.1		9139	59.6		
Yes	11	25.6		102	30.3		192	20.2		246	30.3		5575	42.9		6194	40.4		
Systolic blood pressure (mm Hg)	56		125.5 ± 16.9	363		129.0 ± 19.4	1124		131.8 ± 17.4	888		126.0 ± 16.9	13,945		127.4 ± 17.5	16,608		127.7 ± 17.6
≤120	25	44.6		124	34.2		324	28.8		375	42.2		5340	38.3		6270	37.8		
>120–140	21	37.5		152	41.9		495	44.0		360	40.5		5751	41.2		6873	41.4		
>140	10	17.9		87	24.0		305	27.1		153	17.2		2854	20.5		3465	20.9		
Diastolic blood pressure (mm Hg)	56		75.0 ± 9.4	363		77.5 ± 9.4	1124		78.4 ± 9.2	888		76.0 ± 8.8	13,945		75.4 ± 9.1	16,608		75.7 ± 9.1
<90	52	92.9		324	89.3		982	87.4		828	93.2		12,997	93.2		15,385	92.6		
≥90	*	*		39	10.7		142	12.6		60	6.8		948	6.8		1223	7.4		
History of hypertension																			
Never hypertensive	45	84.9		235	66.4		516	49.8		584	72.8		9097	71.7		10,609	70.0		
Untreated hypertensive	*	*		40	11.3		111	10.7		78	9.7		1015	8.0		1266	8.4		
Treated hypertensive	6	11.3		79	22.3		409	39.5		140	17.5		2571	20.3		3271	21.6		
Treated diabetes (pills or shots)																			
No	50	90.9		332	91.5		990	88.1		826	93.0		13,451	96.5		15,864	95.6		
Yes	5	9.1		31	8.5		134	11.9		62	7.0		487	3.5		734	4.4		
Treated hypercholesterolemia (pills)																			
No	46	90.2		280	80.0		865	84.8		673	85.7		11,061	87.8		13,107	87.3		
Yes	5	9.8		70	20.0		155	15.2		112	14.3		1530	12.2		1906	12.7		
Depression (shortened CES-D/DIS ≥ 0.06)																			
No	44	83.0		331	92.2		923	88.0		616	79.6		12,412	91.1		14,518	90.3		
Yes	*	*		28	7.8		126	12.0		158	20.4		1210	8.9		1563	9.7		

(*continued*)

APPENDIX TABLE 6. *Continued*

Benign breast disease												
No	43	82.7	311	88.1	880	83.9	708	88.7	10,493	82.8	12,618	83.3
Yes, 1 biopsy	8	15.4	32	9.1	132	12.6	71	8.9	1679	13.2	1948	12.9
Yes, 2+ biopsies	*	*	10	2.8	37	3.5	19	2.4	500	3.9	578	3.8
History of cardiovascular disease[d]												
No	50	89.3	348	96.7	1002	91.2	832	95.0	12,940	93.7	15,386	93.7
Yes	6	10.7	12	3.3	97	8.8	44	5.0	868	6.3	1040	6.3
History of MI												
No	53	94.6	362	99.7	1094	97.3	882	99.3	13,694	98.2	16,312	98.2
Yes	*	*	*	*	30	2.7	6	0.7	251	1.8	296	1.8
History of CABG/PTCA												
No	55	100.0	357	99.2	1081	98.5	871	99.5	13,605	98.6	16,191	98.7
Yes	0	0.0	*	*	17	1.5	*	*	189	1.4	215	1.3
History of CHF												
No	56	100.0	361	99.4	1112	98.9	881	99.2	13,886	99.6	16,528	99.5
Yes	0	0.0	*	*	12	1.1	7	0.8	59	0.4	80	0.5
History of angina												
No	53	94.6	354	97.8	1070	96.1	866	98.1	13,512	97.2	16,080	97.1
Yes	*	*	8	2.2	44	3.9	17	1.9	394	2.8	472	2.9
History of carotid endarterectomy/angioplasty												
No	55	100.0	361	100.0	1095	99.7	875	100.0	13,764	99.8	16,374	99.8
Yes	0	0.0	0	0.0	*	*	0	0.0	31	0.2	34	0.2
History of DVT												
No	56	100.0	363	100.0	1122	99.8	884	99.5	13,834	99.2	16,490	99.3
Yes	0	0.0	0	0.0	*	*	*	*	111	0.8	118	0.7
History of PE												
No	56	100.0	362	99.7	1122	99.8	888	100.0	13,920	99.8	16,579	99.8
Yes	0	0.0	*	*	*	*	0	0.0	25	0.2	29	0.2
History of PAD												
No	55	98.2	362	99.7	1103	98.5	871	98.5	13,815	99.3	16,437	99.2
Yes	*	*	*	*	17	1.5	13	1.5	103	0.7	135	0.8
History of stroke												
No	54	96.4	361	99.4	1106	98.4	880	99.1	13,839	99.2	16,470	99.2
Yes	*	*	*	*	18	1.6	8	0.9	106	0.8	138	0.8
History of polyp removal												
No	51	96.2	324	92.6	963	93.9	760	96.3	11,615	92.6	13,911	92.9
Yes	*	*	26	7.4	63	6.1	29	3.7	928	7.4	1068	7.1
History of fracture at age 55+[e]												
No	39	88.6	272	89.8	786	93.0	562	92.0	9,492	83.4	11,317	84.6
Yes	5	11.4	31	10.2	59	7.0	49	8.0	1889	16.6	2057	15.4
History of hip fracture at age 55+[e]												
No	44	100.0	302	99.7	844	99.9	609	99.7	11,301	99.3	13,289	99.4
Yes	*	*	1	0.3	1	0.1	2	0.3	80	0.7	85	0.6

Number of falls in last 12 mo																				
None	38	70.4		272	76.6		716	67.6		572	70.0		8586	66.2		10,340	66.8			
1	9	16.7		57	16.1		226	21.3		158	19.3		2704	20.8		3188	20.6			
2	*	*		19	5.4		89	8.4		49	6.0		1117	8.6		1296	8.4			
3+	*	*		7	2.0		28	2.6		38	4.7		565	4.4		652	4.2			
History of cancer[f]																				
No	55	98.2		357	98.3		1089	98.0		865	98.2		13,567	98.0		16,156	98.0			
Yes	*	*		6	1.7		22	2.0		16	1.8		274	2.0		325	2.0			
History of colorectal cancer																				
No	55	98.2		362	99.7		1121	99.7		888	100.0		13,898	99.7		16,556	99.7			
Yes	*	*		*	*		*	*		0	0.0		47	0.3		52	0.3			
History of melanoma cancer																				
No	56	100.0		363	100.0		1124	100.0		888	100.0		13,944	100.0		16,607	100.0			
Yes	0	0.0		0	0.0		0	0.0		0	0.0		*	*		*	*			
History of cervical cancer																				
No	56	100.0		363	100.0		1110	99.7		881	99.9		13,799	99.8		16,438	99.8			
Yes	0	0.0		0	0.0		*	*		*	*		33	0.2		37	0.2			
History of ovarian cancer																				
No	56	100.0		361	99.7		1112	100.0		881	100.0		13,823	99.9		16,462	100.0			
Yes	0	0.0		*	*		0	0.0		0	0.0		7	0.1		8	0.0			
History of lung cancer																				
No	56	100.0		362	100.0		1112	100.0		882	100.0		13,826	100.0		16,467	100.0			
Yes	0	0.0		0	0.0		0	0.0		0	0.0		5	0.0		5	0.0			
History of osteoporosis																				
No	53	98.1		342	95.3		1052	96.8		809	94.4		13,059	95.0		15,532	95.1			
Yes	*	*		17	4.7		35	3.2		48	5.6		687	5.0		799	4.9			
History of arthritis																				
No arthritis	32	59.3		243	67.9		596	55.5		558	67.1		7963	59.7		9525	60.0			
Rheumatoid arthritis	6	11.1		16	4.5		81	7.5		33	4.0		514	3.9		667	4.2			
Other arthritis	16	29.6		99	27.7		396	36.9		241	29.0		4855	36.4		5682	35.8			
Total hip BMD (WHO criteria)																				
Normal							69	70.4		28	45.9		414	49.1		511	51.0			
Osteopenic							28	28.6		31	50.8		377	44.7		436	43.5			
Osteoporotic							*	*		*	*		52	6.2		55	5.5			
Hip scan (g/cm^2)	12		0.89 ± 0.08	*		*	98		0.97 ± 0.15	61		0.84 ± 0.13	843		0.82 ± 0.12	1024		0.84 ± 0.13		
Spine scan (g/cm^2)	12		0.93 ± 0.11	*		*	99		1.08 ± 0.19	61		0.92 ± 0.14	822		0.93 ± 0.15	1004		0.95 ± 0.16		
Whole body scan (g/cm^2)	12		1.00 ± 0.09	*		*	99		1.08 ± 0.11	61		1.02 ± 0.11	843		0.98 ± 0.09	1025		0.99 ± 0.10		
Lean body mass + BMC (kg)	12		39.8 ± 4.0	*		*	99		44.8 ± 6.5	61		39.0 ± 5.6	834		39.5 ± 5.1	1016		40.0 ± 5.5		
Fat body mass (kg)	12		39.3 ± 11.1	*		*	99		39.0 ± 13.4	61		33.3 ± 8.9	834		31.7 ± 10.7	1016		32.5 ± 11.1		

CABG, coronary bypass surgery; PTCA, angioplasty; WHO, World Health Organization; E + P, estrogen + progestin; E-alone, estrogen alone; BMC, bone mineral content; PHT, postmenopausal hormone therapy; BMD, bone mineral density; MI, myocardial infarction; CHF, congestive heart failure; DVT, deep vein thrombosis; PE, pulmonary embolism; PAD, peripheral arterial disease.

[a]Total includes those of unknown ethnicity.

[b]Applies only to participants who have ever been pregnant.

[c]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.

[d]Includes MI, stroke, CHF, angina, carotid endarterectomy/angioplasty, DVT, PE, PAD, and CABG/PTCA.

[e]Applies only to participants age 55 and older.

[f]Excluding nonmelanoma skin cancer.

*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 7. Baseline medical history status of WHI Estrogen-Alone participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 75)			Asian/Pacific Islander (*N* = 164)			Black (*N* = 1617)			Hispanic (*N* = 655)			White (*N* = 8082)			Total[a] (*N* = 10,739)		
Medical History	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Age at hysterectomy (y)																		
Not hysterectomized																		
<40	36	48.0		53	32.3		783	48.8		278	42.8		3045	37.9		4249	39.8	
40–49	32	42.7		78	47.6		655	40.8		285	43.8		3435	42.7		4556	42.7	
50+	7	9.3		33	20.1		167	10.4		87	13.4		1559	19.4		1872	17.5	
Age at menopause (y)																		
<40	24	39.3		26	19.3		403	29.5		104	19.8		1550	22.3		2139	23.3	
40–49	11	18.0		45	33.3		350	25.6		171	32.6		2146	30.8		2752	30.0	
50+	26	42.6		64	47.4		614	44.9		250	47.6		3269	46.9		4281	46.7	
Bilateral oophorectomy																		
No	34	53.1		80	55.2		838	59.8		395	66.1		4469	58.8		5890	59.3	
Yes	30	46.9		65	44.8		564	40.2		203	33.9		3131	41.2		4049	40.7	
Ever pregnant																		
No	*	*		23	14.0		148	9.2		34	5.2		498	6.2		713	6.7	
Yes	74	98.7		141	86.0		1459	90.8		618	94.8		7567	93.8		9995	93.3	
Age at first birth (y)[b]																		
Never had term pregnancy	*	*		5	4.0		94	7.8		13	2.8		120	1.7		237	2.7	
<20	29	45.3		22	17.5		527	43.7		151	32.6		1660	24.1		2417	27.3	
20–29	33	51.6		82	65.1		530	43.9		270	58.3		4740	68.9		5737	64.8	
30+	*	*		17	13.5		55	4.6		29	6.3		361	5.2		469	5.3	
Number of live births																		
Never pregnant	*	*		23	14.1		148	9.3		34	5.3		498	6.2		713	6.7	
None	*	*		*	*		104	6.5		14	2.2		134	1.7		262	2.5	
1	*	*		10	6.1		229	14.3		51	7.9		550	6.8		862	8.1	
2–4	39	52.0		85	52.1		797	49.8		369	57.0		5212	64.9		6589	61.8	
5+	29	38.7		40	24.5		321	20.1		179	27.7		1641	20.4		2237	21.0	
Number of pregnancies																		
Never pregnant	*	*		23	14.0		148	9.3		34	5.2		498	6.2		713	6.7	
1	*	*		*	*		159	10.0		28	4.3		404	5.0		621	5.8	
2–4	39	52.0		59	36.0		531	33.3		273	42.1		2667	33.1		3615	33.9	
5+	31	41.3		73	44.5		755	47.4		313	48.3		4477	55.6		5722	53.6	
Any induced abortions[b]																		
Pregnant, never had abortion	62	91.2		113	89.0		1134	86.2		456	89.4		6591	94.8		8473	93.1	
One or more abortions	*	*		14	11.0		182	13.8		54	10.6		359	5.2		624	6.9	
Number of months breastfed																		
Never breastfed	33	44.6		67	41.1		760	48.8		268	41.8		3761	47.2		4959	47.0	
1–6	19	25.7		51	31.3		426	27.3		189	29.5		2243	28.2		2964	28.1	
7–12	9	12.2		25	15.3		192	12.3		81	12.6		865	10.9		1190	11.3	
13–23	*	*		8	4.9		91	5.8		53	8.3		643	8.1		811	7.7	
24+	9	12.2		12	7.4		89	5.7		50	7.8		449	5.6		617	5.9	

Age at tubal ligation (y)										
Never had tubal ligation	55	75.3	132	81.5	1294	81.3	524	81.0	6964	86.6	9090	85.3
<30	*	*	*	*	84	5.3	34	5.3	318	4.0	457	4.3
30–34	*	*	*	*	121	7.6	26	4.0	360	4.5	530	5.0
35–39	*	*	14	8.6	68	4.3	48	7.4	286	3.6	426	4.0
40–44	*	*	*	*	21	1.3	13	2.0	97	1.2	135	1.3
45+	0	0.0	0	0.0	*	*	*	*	14	0.2	19	0.2
Age last had any menstrual bleeding (y)										
<40	28	46.7	38	26.4	551	42.7	203	39.2	2318	34.9	3179	36.2
40–44	17	28.3	49	34.0	355	27.5	145	28.0	1694	25.5	2297	26.2
45–49	8	13.3	35	24.3	244	18.9	108	20.8	1476	22.2	1901	21.7
50–54	6	10.0	18	12.5	106	8.2	50	9.7	902	13.6	1096	12.5
55–59	*	*	*	*	25	1.9	11	2.1	202	3.0	244	2.8
60+	0	0.0	*	*	10	0.8	*	*	49	0.7	63	0.7
Current health care provider										
No	7	9.6	10	6.2	173	11.0	175	27.2	794	9.9	1175	11.1
Yes	66	90.4	152	93.8	1406	89.0	469	72.8	7207	90.1	9425	88.9
Mammogram in last 2 y										
No	26	37.7	54	34.6	406	27.6	245	40.0	2260	28.9	3035	29.6
Yes	43	62.3	102	65.4	1063	72.4	367	60.0	5547	71.1	7220	70.4
Total oral contraceptive duration (y)										
Nonuser	47	62.7	110	67.1	1072	66.3	385	58.8	4917	60.8	6634	61.8
<5	23	30.7	32	19.5	286	17.7	167	25.5	1876	23.2	2409	22.4
5–<10	*	*	*	*	133	8.2	58	8.9	699	8.6	914	8.5
10+	*	*	13	7.9	126	7.8	45	6.9	590	7.3	782	7.3
History of PHT use[c]										
Never	40	53.3	74	45.1	978	60.7	394	60.2	3892	48.2	5447	50.8
Past	27	36.0	60	36.6	450	27.9	155	23.7	2918	36.1	3669	34.2
Current	8	10.7	30	18.3	184	11.4	106	16.2	1262	15.6	1608	15.0
Total PHT duration (y)										
Nonuser	40	53.3	74	45.1	978	60.5	394	60.2	3892	48.2	5447	50.7
<5	18	24.0	48	29.3	397	24.6	157	24.0	2196	27.2	2853	26.6
5–<10	8	10.7	18	11.0	96	5.9	52	7.9	808	10.0	995	9.3
10–<15	*	*	10	6.1	78	4.8	21	3.2	534	6.6	660	6.1
15+	6	8.0	14	8.5	68	4.2	31	4.7	652	8.1	784	7.3
History of E-alone use[c]										
Never	40	53.3	80	48.8	1005	62.3	410	62.6	4056	50.2	5664	52.8
Past	27	36.0	55	33.5	430	26.7	143	21.8	2802	34.7	3513	32.8
Current	8	10.7	29	17.7	177	11.0	102	15.6	1215	15.1	1548	14.4
Total E-alone duration (y)[c]										
Nonuser	40	53.3	80	48.8	1005	62.2	410	62.6	4056	50.2	5664	52.7
<5	18	24.0	45	27.4	386	23.9	149	22.7	2152	26.6	2787	26.0
5–<10	8	10.7	15	9.1	89	5.5	47	7.2	776	9.6	947	8.8
10–<15	*	*	10	6.1	75	4.6	21	3.2	491	6.1	612	5.7
15+	6	8.0	14	8.5	62	3.8	28	4.3	607	7.5	729	6.8
History of E + P use[c]										
Never	75	100.0	155	94.5	1564	96.7	628	95.9	7700	95.3	10,261	95.6
Past	0	0.0	7	4.3	43	2.7	23	3.5	329	4.1	408	3.8
Current	0	0.0	*	*	10	0.6	*	*	52	0.6	69	0.6

(*continued*)

APPENDIX TABLE 7. *Continued*

Total E + P duration (y)[c]																
Nonuser	75	100.0		155	94.5		1564	96.7		628	95.9		7700	95.3		10,261	95.5	
<5	0	0.0		6	3.7		35	2.2		18	2.7		249	3.1		312	2.9	
5–<10	0	0.0		*	*		11	0.7		5	0.8		78	1.0		97	0.9	
10–<15	0	0.0		0	0.0		*	*		*	*		30	0.4		40	0.4	
15+	0	0.0		0	0.0		*	*		*	*		25	0.3		29	0.3	
Family history of MI																		
No	26	36.1		74	50.3		779	54.4		337	55.3		3333	43.6		4616	46.0	
Yes	46	63.9		73	49.7		653	45.6		272	44.7		4303	56.4		5414	54.0	
Family history of breast cancer																		
No	50	72.5		135	87.7		1239	83.9		541	87.8		6233	81.8		8309	82.5	
Yes	19	27.5		19	12.3		238	16.1		75	12.2		1390	18.2		1763	17.5	
Family history of colorectal cancer																		
No	59	89.4		123	83.1		1110	83.0		505	86.2		6014	82.1		7921	82.6	
Yes	7	10.6		25	16.9		228	17.0		81	13.8		1313	17.9		1673	17.4	
Family history of stroke																		
No	39	55.7		95	64.2		855	58.0		402	66.3		4553	60.1		6033	60.3	
Yes	31	44.3		53	35.8		620	42.0		204	33.7		3017	39.9		3970	39.7	
Family history of adult diabetes																		
No	33	45.8		88	59.9		636	44.6		315	52.4		4919	64.5		6065	60.6	
Yes	39	54.2		59	40.1		789	55.4		286	47.6		2709	35.5		3941	39.4	
Parent broke bone after age 40																		
No	51	70.8		104	69.8		1106	81.0		395	67.9		4378	58.9		6119	63.0	
Yes	21	29.2		45	30.2		259	19.0		187	32.1		3055	41.1		3600	37.0	
Systolic blood pressure (mm Hg)	75		132.7 ± 18.4	164		134.7 ± 18.7	1617		134.3 ± 17.5	655		128.0 ± 16.7	8082		129.5 ± 17.4	10,739		130.3 ± 17.5
≤120	17	22.7		41	25.0		385	23.8		232	35.4		2676	33.1		3394	31.6	
>120–140	35	46.7		65	39.6		709	43.8		279	42.6		3505	43.4		4641	43.2	
>140	23	30.7		58	35.4		523	32.3		144	22.0		1901	23.5		2704	25.2	
Diastolic blood pressure (mm Hg)	75		77.8 ± 9.1	164		79.8 ± 10.4	1616		79.3 ± 9.4	655		75.9 ± 9.4	8081		75.9 ± 9.1	10,737		76.5 ± 9.3
<90	67	89.3		135	82.3		1372	84.9		605	92.4		7499	92.8		9799	91.3	
≥90	8	10.7		29	17.7		244	15.1		50	7.6		582	7.2		938	8.7	
History of hypertension																		
Never hypertensive	35	50.0		85	53.5		597	40.3		397	66.9		4569	63.3		5762	59.7	
Untreated hypertensive	11	15.7		16	10.1		177	12.0		73	12.3		700	9.7		993	10.3	
Treated hypertensive	24	34.3		58	36.5		707	47.7		123	20.7		1948	27.0		2903	30.1	
Treated diabetes (pills or shots)																		
No	62	82.7		146	89.0		1397	86.7		590	90.1		7580	93.9		9907	92.3	
Yes	13	17.3		18	11.0		215	13.3		65	9.9		496	6.1		821	7.7	
Treated hypercholesterolemia (pills)																		
No	60	88.2		117	74.1		1223	83.9		485	84.3		6152	85.3		8147	84.8	
Yes	8	11.8		41	25.9		234	16.1		90	15.7		1058	14.7		1460	15.2	
Depression (shortened CES-D/DIS ≥ 0.06)																		
No	60	82.2		138	86.8		1253	82.8		454	78.4		6930	88.0		8959	86.7	
Yes	13	17.8		21	13.2		261	17.2		125	21.6		941	12.0		1375	13.3	

Benign breast disease												
No	60	85.7	130	81.8	1212	81.7	489	83.4	5683	78.6	7681	79.5
Yes, 1 biopsy	9	12.9	13	8.2	215	14.5	62	10.6	1116	15.4	1439	14.9
Yes, 2+ biopsies	*	*	16	10.1	57	3.8	35	6.0	427	5.9	545	5.6
History of cardiovascular disease[d]												
No	61	82.4	154	93.9	1352	85.2	588	91.6	7150	89.3	9433	88.8
Yes	13	17.6	10	6.1	234	14.8	54	8.4	858	10.7	1184	11.2
History of MI												
No	72	96.0	163	99.4	1549	95.8	648	98.9	7828	96.9	10,402	96.9
Yes	*	*	*	*	68	4.2	7	1.1	254	3.1	337	3.1
History of CABG/PTCA												
No	72	97.3	161	98.2	1543	97.8	630	98.6	7799	97.7	10,345	97.8
Yes	*	*	*	*	35	2.2	9	1.4	182	2.3	234	2.2
History of CHF												
No	75	100.0	164	100.0	1588	98.2	651	99.4	8018	99.2	10,640	99.1
Yes	0	0.0	0	0.0	29	1.8	*	*	64	0.8	99	0.9
History of angina												
No	69	92.0	154	93.9	1498	93.3	625	95.6	7595	94.3	10,079	94.3
Yes	6	8.0	10	6.1	108	6.7	29	4.4	455	5.7	614	5.7
History of carotid endarterectomy/angioplasty												
No	74	100.0	164	100.0	1572	99.6	639	99.8	7951	99.6	10,543	99.6
Yes	0	0.0	0	0.0	6	0.4	*	*	31	0.4	38	0.4
History of DVT												
No	74	98.7	164	100.0	1604	99.2	649	99.1	7954	98.4	10,590	98.6
Yes	*	*	0	0.0	13	0.8	6	0.9	128	1.6	149	1.4
History of PE												
No	75	100.0	164	100.0	1612	99.7	655	100.0	8055	99.7	10,707	99.7
Yes	0	0.0	0	0.0	5	0.3	0	0.0	27	0.3	32	0.3
History of PAD												
No	74	98.7	164	100.0	1567	97.6	640	98.2	7943	98.6	10,531	98.5
Yes	*	*	0	0.0	38	2.4	12	1.8	110	1.4	162	1.5
History of stroke												
No	70	93.3	163	99.4	1573	97.3	645	98.5	7979	98.7	10,571	98.4
Yes	5	6.7	*	*	44	2.7	10	1.5	103	1.3	168	1.6
History of polyp removal												
No	62	88.6	138	87.3	1330	90.8	547	93.3	6456	90.0	8659	90.3
Yes	8	11.4	20	12.7	134	9.2	39	6.7	714	10.0	926	9.7
History of fracture at age 55+[e]												
No	48	73.8	116	90.6	1106	90.9	403	90.0	5390	82.8	7168	84.5
Yes	17	26.2	12	9.4	111	9.1	45	10.0	1116	17.2	1319	15.5
History of hip fracture at age 55+[e]												
No	65	100.0	127	99.2	1212	99.6	444	99.1	6,463	99.3	8,433	99.4
Yes	*	*	1	0.8	5	0.4	4	0.9	43	0.7	54	0.6
Number of falls in last 12 mo												
None	47	65.3	118	73.8	1054	69.4	397	65.8	4815	64.9	6530	65.9
1	13	18.1	28	17.5	272	17.9	101	16.7	1562	21.1	1999	20.2
2	5	6.9	9	5.6	129	8.5	63	10.4	682	9.2	900	9.1
3+	7	9.7	5	3.1	64	4.2	42	7.0	361	4.9	486	4.9
History of cancer[f]												
No	74	98.7	149	92.5	1530	96.0	623	96.3	7566	94.5	10,078	94.8
Yes	*	*	12	7.5	63	4.0	24	3.7	441	5.5	549	5.2

(*continued*)

APPENDIX TABLE 7. *Continued*

History of colorectal cancer																						
No	75	100.0		162	98.8		1615	99.9		655	100.0		8052	99.6		10,704	99.7				
Yes	0	0.0		*	*		*	*		0	0.0		30	0.4		35	0.3				
History of endometrial cancer																						
No	75	100.0		164	100.0		1617	100.0		654	99.8		8081	100.0		10,737	100.0				
Yes	0	0.0		0	0.0		0	0.0		*	*		*	*		*	*				
History of cervical cancer																						
No	75	100.0		159	99.4		1578	98.8		637	98.5		7802	97.7		10,392	97.9				
Yes	0	0.0		*	*		19	1.2		10	1.5		186	2.3		219	2.1				
History of ovarian cancer																						
No	75	100.0		159	98.8		1584	99.2		645	99.7		7947	99.4		10,554	99.4				
Yes	0	0.0		*	*		12	0.8		*	*		47	0.6		63	0.6				
History of lung cancer																						
No	75	100.0		159	99.4		1593	99.8		646	99.8		7984	99.9		10,601	99.9				
Yes	0	0.0		*	*		*	*		*	*		*	*		9	0.1				
History of osteoporosis																						
No	66	93.0		157	96.9		1494	95.8		569	90.9		7458	93.5		9880	93.8				
Yes	5	7.0		5	3.1		65	4.2		57	9.1		519	6.5		658	6.2				
History of arthritis																						
No arthritis	36	50.7		101	63.5		709	46.5		342	56.9		3821	50.3		5090	50.4				
Rheumatoid arthritis	7	9.9		8	5.0		162	10.6		48	8.0		400	5.3		631	6.3				
Other arthritis	28	39.4		50	31.4		655	42.9		211	35.1		3377	44.4		4373	43.3				
Total hip BMD (WHO criteria)																						
Normal							112	64.4		41	63.1		345	50.5		498	54.0				
Osteopenic							61	35.1		20	30.8		286	41.9		367	39.8				
Osteoporotic							*	*		*	*		52	7.6		57	6.2				
Hip scan (g/cm^2)	7		0.99 ± 0.19	*		*	174		0.96 ± 0.13	65		0.87 ± 0.11	683		0.83 ± 0.13	934		0.86 ± 0.14			
Spine scan (g/cm^2)	7		1.04 ± 0.22	*		*	171		1.04 ± 0.15	65		0.96 ± 0.13	663		0.95 ± 0.16	911		0.97 ± 0.16			
Whole body scan (g/cm^2)	7		1.06 ± 0.13	*		*	174		1.06 ± 0.10	66		1.03 ± 0.10	685		0.99 ± 0.10	937		1.01 ± 0.11			
Lean body mass + BMC (kg)	7		42.0 ± 6.6	*		*	174		44.5 ± 5.9	66		39.4 ± 4.8	676		39.9 ± 5.6	928		40.7 ± 5.9			
Fat body mass (kg)	7		44.6 ± 13.6	*		*	174		40.4 ± 12.6	66		35.9 ± 9.5	676		34.6 ± 10.9	928		35.8 ± 11.4			

CABG, coronary bypass surgery; PTCA, angioplasty; WHO, World Health Organization; E + P, estrogen + progestin; E-alone, estrogen alone; BMC, bone mineral content; PHT, postmenopausal hormone therapy; BMD, bone mineral density; MI, myocardial infarction; CHF, congestive heart failure; DVT, deep vein thrombosis; PE, pulmonary embolism; PAD, peripheral arterial disease.

[a]Total includes those of unknown ethnicity.

[b]Applies only to participants who have ever been pregnant.

[c]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.

[d]Includes MI, stroke, CHF, angina, carotid endarterectomy/angioplasty, DVT, PE, peripheral arterial disease, and CABG/PTCA.

[e]Applies only to participants age 55 and older.

[f]Excluding nonmelanoma skin cancer.

*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 8. Baseline medical history status of WHI Dietary Modification participants by race/ethnicity

	Race/Ethnicity																			
	American Indian (*N* = 203)			Asian/Pacific Islander (*N* = 1107)			Black (*N* = 5266)			Hispanic (*N* = 1854)			White (*N* = 39,760)			Total[a] (*N* = 48,836)		
Medical History	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Hysterectomy[b]																		
No	95	46.8		701	63.3		2354	44.7		989	53.3		23,136	58.2		27,634	56.6	
Yes	108	53.2		406	36.7		2912	55.3		865	46.7		16,624	41.8		21,202	43.4	
Age at hysterectomy (y)																		
Not hysterectomized	95	47.3		701	63.4		2354	44.9		989	53.5		23,136	58.3		27,634	56.7	
<40	47	23.4		100	9.0		1318	25.1		346	18.7		5327	13.4		7245	14.9	
40–49	44	21.9		214	19.4		1233	23.5		362	19.6		7373	18.6		9350	19.2	
50+	15	7.5		90	8.1		338	6.4		151	8.2		3853	9.7		4502	9.2	
Age at menopause (y)																		
<40	34	18.4		68	6.4		732	15.6		185	11.2		3456	9.3		4542	10.0	
40–49	78	42.2		574	54.2		2042	43.4		780	47.3		19,165	51.4		22,914	50.4	
50+	73	39.5		418	39.4		1933	41.1		684	41.5		14,648	39.3		18,008	39.6	
Bilateral oophorectomy																		
No	149	76.4		852	78.3		3835	77.5		1427	80.0		31,104	79.6		37,855	79.3	
Yes	46	23.6		236	21.7		1115	22.5		357	20.0		7990	20.4		9881	20.7	
Ever pregnant																		
No	*	*		134	12.1		373	7.1		128	6.9		3404	8.6		4100	8.4	
Yes	197	97.0		973	87.9		4873	92.9		1715	93.1		36,304	91.4		44,650	91.6	
Age at first birth (y)[c]																		
Never had term pregnancy	5	2.8		34	3.9		278	6.9		53	4.0		840	2.5		1228	3.0	
<20	55	31.1		55	6.3		1404	34.6		321	24.2		4938	14.8		6892	17.1	
20–29	105	59.3		651	74.5		2078	51.2		835	63.0		24,792	74.3		28,798	71.5	
30+	12	6.8		134	15.3		298	7.3		116	8.8		2779	8.3		3380	8.4	
Number of live births																		
Never pregnant	*	*		134	12.1		373	7.1		128	7.0		3404	8.6		4100	8.4	
None	*	*		37	3.3		291	5.6		57	3.1		881	2.2		1290	2.7	
1	25	12.3		108	9.8		819	15.7		176	9.6		3101	7.8		4291	8.8	
2–4	128	63.1		731	66.2		2877	55.1		1092	59.7		26,447	66.8		31,669	65.2	
5+	39	19.2		95	8.6		864	16.5		377	20.6		5760	14.5		7242	14.9	
Number of pregnancies																		
Never pregnant	*	*		134	12.1		373	7.1		128	7.0		3404	8.6		4100	8.4	
1	17	8.4		86	7.8		515	9.9		122	6.6		2510	6.3		3293	6.8	
2–4	70	34.5		174	15.7		1614	30.9		647	35.3		10,049	25.3		12,747	26.2	
5+	110	54.2		712	64.4		2720	52.1		938	51.1		23,697	59.8		28,529	58.6	
Any induced abortions[c]																		
Pregnant, never had abortion	156	89.1		845	90.1		3686	82.6		1294	86.3		31,587	92.9		38,044	91.5	
One or more abortions	19	10.9		93	9.9		778	17.4		206	13.7		2401	7.1		3556	8.5	
Number of months breastfed																		
Never breastfed	79	39.5		456	41.4		2731	52.9		829	45.6		19,181	48.7		23,569	48.8	
1–6	64	32.0		323	29.3		1393	27.0		519	28.5		10,039	25.5		12,510	25.9	
7–12	19	9.5		163	14.8		530	10.3		203	11.2		4367	11.1		5353	11.1	
13–23	16	8.0		88	8.0		292	5.7		153	8.4		3585	9.1		4191	8.7	
24+	22	11.0		71	6.4		213	4.1		115	6.3		2186	5.6		2653	5.5	

(*continued*)

APPENDIX TABLE 8. *Continued*

Age at tubal ligation (y)												
Never had tubal ligation	151	75.1	852	77.3	3967	76.3	1425	77.8	32,718	82.7	39,629	81.6
<30	10	5.0	34	3.1	235	4.5	75	4.1	940	2.4	1316	2.7
30–34	15	7.5	80	7.3	407	7.8	106	5.8	1871	4.7	2519	5.2
35–39	14	7.0	99	9.0	409	7.9	141	7.7	2345	5.9	3050	6.3
40–44	10	5.0	32	2.9	161	3.1	71	3.9	1384	3.5	1674	3.4
45+	*	*	*	*	19	0.4	14	0.8	307	0.8	351	0.7
Age last had any menstrual bleeding (y)												
<40	40	24.4	105	10.1	1004	22.6	265	17.8	4242	12.8	5739	14.0
40–44	22	13.4	146	14.1	817	18.4	242	16.3	4495	13.5	5802	14.2
45–49	35	21.3	237	22.9	957	21.5	337	22.7	7145	21.5	8836	21.6
50–54	53	32.3	398	38.4	1136	25.5	473	31.8	11,488	34.6	13,722	33.5
55–60	11	6.7	118	11.4	428	9.6	136	9.1	4303	13.0	5062	12.4
60+	*	*	33	3.2	110	2.5	34	2.3	1547	4.7	1749	4.3
Current health care provider												
No	6	3.0	52	4.7	418	8.1	343	18.8	2195	5.6	3048	6.3
Yes	195	97.0	1053	95.3	4732	91.9	1479	81.2	37,278	94.4	45,344	93.7
Mammogram in last 2 y												
No	32	17.2	194	18.0	925	18.7	471	27.2	6106	15.8	7834	16.6
Yes	154	82.8	884	82.0	4023	81.3	1258	72.8	32,595	84.2	39,438	83.4
Pap smear in last 3 y												
No	11	13.3	96	14.7	247	12.9	137	17.5	2015	10.6	2550	11.2
Yes	72	86.7	555	85.3	1663	87.1	645	82.5	16,991	89.4	20,198	88.8
Total oral contraceptive duration (y)												
Nonuser	100	49.3	642	58.0	3068	58.3	1011	54.5	21,906	55.1	27,092	55.5
<5	61	30.0	266	24.0	1068	20.3	480	25.9	9877	24.8	11,915	24.4
5–<10	20	9.9	105	9.5	568	10.8	212	11.4	4096	10.3	5065	10.4
10+	22	10.8	94	8.5	562	10.7	151	8.1	3881	9.8	4764	9.8
History of PHT use[d]												
Never	91	44.8	400	36.2	3063	58.3	882	47.7	15,111	38.1	19,809	40.6
Past	35	17.2	127	11.5	755	14.4	246	13.3	5504	13.9	6765	13.9
Current	77	37.9	579	52.4	1438	27.4	721	39.0	19,089	48.1	22,190	45.5
Total PHT duration (y)[d]												
Nonuser	91	44.8	400	36.1	3063	58.2	882	47.6	15,111	38.0	19,809	40.6
<5	41	20.2	287	25.9	1169	22.2	487	26.3	9467	23.8	11,620	23.8
5–<10	28	13.8	179	16.2	433	8.2	205	11.1	5627	14.2	6552	13.4
10–<15	21	10.3	113	10.2	267	5.1	125	6.7	4106	10.3	4685	9.6
15+	22	10.8	128	11.6	334	6.3	155	8.4	5449	13.7	6170	12.6

History of E-alone use[d]																			
Never	123	60.6		725	65.6		3527	67.1		1221	66.0		24,318	61.2		30,319	62.2		
Past	29	14.3		92	8.3		632	12.0		172	9.3		4600	11.6		5606	11.5		
Current	51	25.1		289	26.1		1097	20.9		456	24.7		10,800	27.2		12,853	26.3		
Total E-alone duration (y)[d]																			
Nonuser	123	60.6		725	65.5		3527	67.0		1221	65.9		24,318	61.2		30,319	62.1		
<5	29	14.3		136	12.3		903	17.1		293	15.8		5638	14.2		7099	14.5		
5–<10	18	8.9		84	7.6		335	6.4		132	7.1		2993	7.5		3609	7.4		
10–<15	14	6.9		63	5.7		219	4.2		80	4.3		2461	6.2		2872	5.9		
15+	19	9.4		99	8.9		282	5.4		128	6.9		4350	10.9		4937	10.1		
History of E + P use[d]																			
Never	161	79.3		723	65.3		4654	88.4		1453	78.4		27,774	69.9		35,232	72.2		
Past	15	7.4		89	8.0		261	5.0		130	7.0		3458	8.7		4006	8.2		
Current	27	13.3		295	26.6		350	6.6		271	14.6		8498	21.4		9567	19.6		
Total E + P duration (y)[d]																			
Nonuser	161	79.3		723	65.3		4654	88.4		1453	78.4		27,774	69.9		35,232	72.1		
<5	21	10.3		201	18.2		399	7.6		254	13.7		6264	15.8		7238	14.8		
5–<10	11	5.4		108	9.8		131	2.5		81	4.4		3306	8.3		3679	7.5		
10–<15	8	3.9		53	4.8		51	1.0		46	2.5		1663	4.2		1846	3.8		
15+	*	*		22	2.0		30	0.6		20	1.1		753	1.9		840	1.7		
Family history of MI																			
No	92	48.7		682	65.8		2658	55.5		968	55.9		17,475	46.1		22,162	47.9		
Yes	97	51.3		354	34.2		2128	44.5		763	44.1		20,421	53.9		24,065	52.1		
Family history of breast cancer																			
No	153	80.5		908	85.0		4163	85.4		1536	87.6		30,719	81.3		37,963	82.0		
Yes	37	19.5		160	15.0		714	14.6		217	12.4		7081	18.7		8325	18.0		
Family history of colorectal cancer																			
No	146	82.0		857	83.0		3819	84.4		1482	88.6		30,645	83.4		37,427	83.7		
Yes	32	18.0		175	17.0		707	15.6		190	11.4		6085	16.6		7285	16.3		
Family history of stroke																			
No	109	58.6		585	55.3		2911	59.5		1116	65.3		23,471	62.3		28,578	62.0		
Yes	77	41.4		472	44.7		1978	40.5		593	34.7		14,200	37.7		17,525	38.0		
Family history of adult diabetes																			
No	94	50.8		594	57.6		2273	48.1		927	53.4		25,784	67.9		30,027	64.9		
Yes	91	49.2		437	42.4		2454	51.9		808	46.6		12,209	32.1		16,226	35.1		
Parent broke bone after age 40																			
No	108	63.2		688	67.3		3536	78.4		1160	69.7		21,196	57.2		27,077	60.2		
Yes	63	36.8		335	32.7		972	21.6		504	30.3		15,854	42.8		17,907	39.8		
Systolic blood pressure (mm Hg)	203		127.4 ± 16.2	1107		130.2 ± 17.8	5266.0		132.1 ± 17.0	1854		126.2 ± 16.8	39,758		127.1 ± 17.2	48,834		127.7 ± 17.2	
≥120	73	36.0		343	31.0		1440	27.3		783	42.2		15,232	38.3		18,098	37.1		
>120–140	89	43.8		487	44.0		2375	45.1		740	39.9		16,578	41.7		20,530	42.0		
>140	41	20.2		277	25.0		1451	27.6		331	17.9		7948	20.0		10,206	20.9		
Diastolic blood pressure (mm Hg)	203		76.6 ± 9.1	1107		79.3 ± 9.4	5266.0		78.6 ± 9.3	1854		75.6 ± 8.9	39,747		75.5 ± 9.0	48,823		75.9 ± 9.1	
<90	188	92.6		941	85.0		4573	86.8		1726	93.1		37,191	93.6		45,193	92.6		
≥90	15	7.4		166	15.0		693	13.2		128	6.9		2556	6.4		3630	7.4		

(*continued*)

APPENDIX TABLE 8. *Continued*

History of hypertension										
Never hypertensive	112	60.9	676	62.7	2158	44.7	1146	69.0	23,530	67.2	27,981	64.5
Untreated hypertensive	13	7.1	69	6.4	467	9.7	151	9.1	2749	7.9	3503	8.1
Treated hypertensive	59	32.1	333	30.9	2204	45.6	364	21.9	8739	25.0	11,883	27.4
Treated diabetes (pills or shots)										
No	188	92.6	1041	94.0	4654	88.4	1738	93.8	38,400	96.6	46,629	95.5
Yes	15	7.4	66	6.0	612	11.6	115	6.2	1356	3.4	2202	4.5
Treated hypercholesterolemia (pills)										
No	166	89.7	883	82.3	4135	86.4	1439	88.3	30,857	88.4	37,993	88.0
Yes	19	10.3	190	17.7	653	13.6	191	11.7	4040	11.6	5172	12.0
Depression (shortened CES-D/DIS ≥ 0.06)										
No	158	81.9	1018	93.4	4359	87.1	1388	82.1	35,099	90.1	42,573	89.5
Yes	35	18.1	72	6.6	646	12.9	302	17.9	3846	9.9	4985	10.5
Benign breast disease										
No	145	78.8	886	82.2	3935	80.7	1362	82.4	27,588	78.7	34,372	79.1
Yes, 1 biopsy	28	15.2	143	13.3	690	14.1	196	11.9	5349	15.3	6505	15.0
Yes, 2+ biopsies	11	6.0	49	4.5	252	5.2	94	5.7	2109	6.0	2561	5.9
History of cardiovascular disease[e]										
No	171	84.7	1046	94.9	4484	86.7	1667	91.2	35,364	90.0	43,303	89.7
Yes	31	15.3	56	5.1	689	13.3	160	8.8	3950	10.0	4950	10.3
History of MI										
No	198	97.5	1096	99.0	5115	97.1	1833	98.9	39,051	98.2	47,925	98.1
Yes	5	2.5	11	1.0	151	2.9	21	1.1	709	1.8	911	1.9
History of CABG/PTCA										
No	200	98.5	1095	99.4	5071	98.5	1805	99.0	38,818	98.9	47,617	98.8
Yes	*	*	7	0.6	79	1.5	18	1.0	447	1.1	562	1.2
History of CHF										
No	197	97.0	1103	99.6	5181	98.4	1840	99.2	39,540	99.4	48,502	99.3
Yes	6	3.0	*	*	85	1.6	14	0.8	219	0.6	333	0.7
History of angina										
No	191	94.1	1076	97.4	4965	94.9	1790	96.9	38,224	96.5	46,860	96.3
Yes	12	5.9	29	2.6	268	5.1	57	3.1	1397	3.5	1791	3.7
History of carotid endarterectomy/angioplasty										
No	203	100.0	1102	100.0	5139	99.7	1823	99.9	39,195	99.8	48,097	99.8
Yes	0	0.0	0	0.0	13	0.3	*	*	80	0.2	94	0.2

History of DVT												
No	194	95.6	1098	99.2	5090	96.7	1808	97.5	38,275	96.3	47,087	96.5
Yes	9	4.4	9	0.8	173	3.3	46	2.5	1469	3.7	1729	3.5
History of PE												
No	200	98.5	1103	99.7	5202	98.8	1846	99.6	39,408	99.1	48,401	99.1
Yes	*	*	*	*	63	1.2	7	0.4	341	0.9	421	0.9
History of PAD												
No	197	97.5	1102	99.6	5133	98.1	1815	98.2	39,223	98.9	48,105	98.8
Yes	5	2.5	*	*	97	1.9	34	1.8	423	1.1	568	1.2
History of stroke												
No	199	98.0	1097	99.1	5163	98.0	1827	98.5	39,375	99.0	48,303	98.9
Yes	*	*	10	0.9	103	2.0	27	1.5	385	1.0	533	1.1
History of polyp removal												
No	167	91.3	980	91.4	4424	92.3	1548	94.5	31,638	91.3	39,294	91.6
Yes	16	8.7	92	8.6	367	7.7	90	5.5	3001	8.7	3621	8.4
History of fracture at age 55+[f]												
No	142	91.0	751	90.6	3572	91.9	1173	91.1	26,435	85.2	32,506	86.3
Yes	14	9.0	78	9.4	314	8.1	115	8.9	4591	14.8	5176	13.7
History of hip fracture at age 55+[f]												
No	156	100.0	829	100.0	3877	99.8	1281	99.5	30,855	99.4	37,490	99.5
Yes	*	*	*	*	9	0.2	7	0.5	171	0.6	192	0.5
Number of falls in last 12 mo												
None	117	61.9	838	77.4	3500	70.7	1147	68.1	23,984	66.5	30,011	67.3
1	46	24.3	171	15.8	879	17.8	319	18.9	7522	20.9	9039	20.3
2	15	7.9	58	5.4	411	8.3	140	8.3	3091	8.6	3771	8.5
3+	11	5.8	16	1.5	157	3.2	78	4.6	1467	4.1	1755	3.9
History of cancer[g]												
No	185	92.0	1062	96.7	5001	96.3	1769	96.6	37,581	95.4	46,201	95.6
Yes	16	8.0	36	3.3	191	3.7	63	3.4	1799	4.6	2139	4.4
History of endometrial cancer												
No	199	98.0	1103	99.6	5212	99.0	1839	99.2	39,334	98.9	48,324	99.0
Yes	*	*	*	*	54	1.0	15	0.8	426	1.1	512	1.0
History of melanoma cancer												
No	201	99.0	1107	100.0	5264	100.0	1844	99.5	39,440	99.2	48,502	99.3
Yes	*	*	0	0.0	*	*	10	0.5	319	0.8	333	0.7
History of cervical cancer												
No	197	99.0	1092	99.7	5119	98.6	1818	99.0	38,830	98.7	47,683	98.8
Yes	*	*	*	*	73	1.4	18	1.0	498	1.3	603	1.2
History of ovarian cancer												
No	198	99.5	1090	99.5	5168	99.5	1834	99.9	39,183	99.6	48,106	99.6
Yes	*	*	6	0.5	26	0.5	*	*	158	0.4	195	0.4
History of lung cancer												
No	199	100.0	1093	99.8	5193	100.0	1835	100.0	39,303	99.9	48,258	99.9
Yes	0	0.0	*	*	*	*	*	*	23	0.1	28	0.1

(*continued*)

APPENDIX TABLE 8. *Continued*

History of osteoporosis																
No	190	95.0		1036	94.4		4925	96.1		1665	92.7		36,820	93.8		45,220	94.0	
Yes	10	5.0		62	5.6		201	3.9		131	7.3		2427	6.2		2878	6.0	
History of arthritis																		
No arthritis	86	45.3		749	68.7		2586	51.7		1068	61.7		21,379	57.1		26,210	56.9	
Rheumatoid arthritis	19	10.0		45	4.1		367	7.3		91	5.3		1414	3.8		1974	4.3	
Other arthritis	85	44.7		297	27.2		2045	40.9		573	33.1		14,643	39.1		17,883	38.8	
Total hip BMD (WHO criteria)																		
Normal							413	70.7		119	61.0		1614	58.0		2146	60.2	
Osteopenic							160	27.4		65	33.3		1051	37.8		1276	35.8	
Osteoporotic							11	1.9		11	5.6		119	4.3		141	4.0	
Hip scan (g/cm^2)	29		0.89 ± 0.14	6		0.84 ± 0.12	584		0.97 ± 0.15	195		0.88 ± 0.14	2784		0.85 ± 0.13	3620		0.87 ± 0.14
Spine scan (g/cm^2)	29		0.96 ± 0.15	6		0.97 ± 0.23	581		1.07 ± 0.18	190		0.98 ± 0.16	2723		0.98 ± 0.16	3551		0.99 ± 0.17
Whole body scan (g/cm^2)	29		1.03 ± 0.11	6		1.01 ± 0.12	582		1.07 ± 0.11	195		1.05 ± 0.11	2786		1.01 ± 0.11	3620		1.03 ± 0.11
Lean body mass + BMC (kg)	27		39.4 ± 4.9	6		34.1 ± 4.0	581		44.3 ± 6.5	193		39.3 ± 5.2	2751		39.7 ± 5.2	3580		40.5 ± 5.7
Fat body mass (kg)	27		35.8 ± 11.6	6		22.8 ± 9.7	581		41.0 ± 13.1	193		34.6 ± 9.8	2751		33.4 ± 10.6	3580		34.7 ± 11.4

CABG, coronary bypass surgery; PTCA, angioplasty; WHO, World Health Organization; E+P, estrogen+progestin; E-alone, estrogen alone; BMC, bone mineral content; PHT, postmenopausal hormone therapy; BMD, bone mineral density; MI, myocardial infarction; CHF, congestive heart failure; DVT, deep vein thrombosis; PE, pulmonary embolism; PAD, peripheral arterial disease.

[a]Total includes those of unknown ethnicity.

[b]Hysterectomy at randomization.

[c]Applies only to participants who have ever been pregnant.

[d]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.

[e]Includes MI, stroke, CHF, angina, carotid endarterectomy/angioplasty, DVT, PE, PAD, and CABG/PTCA.

[f]Applies only to participants age 55 and older.

[g]Excluding nonmelanoma skin cancer.

*Data withheld from cells where $N < 5$ (<10 where data are sensitive).

APPENDIX TABLE 9. Baseline medical history status of WHI Calcium and Vitamin D participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 149)			Asian/Pacific Islander (*N* = 722)			Black (*N* = 3317)			Hispanic (*N* = 1507)			White (*N* = 30,153)			Total[a] (*N* = 36,282)		
Medical History	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	N	%	Mean ± SD	*N*	%	Mean ± SD	N	%	Mean ± SD
Hysterectomy[b]																		
No	65	43.6		469	65.0		1432	43.2		827	54.9		18,120	60.1		21,162	58.3	
Yes	84	56.4		253	35.0		1885	56.8		680	45.1		12,032	39.9		15,120	41.7	
Age at hysterectomy (y)																		
Not hysterectomized	65	43.9		469	65.1		1432	43.3		827	55.0		18,120	60.2		21,161	58.5	
<40	32	21.6		75	10.4		859	26.0		282	18.8		4081	13.6		5404	14.9	
40–49	41	27.7		117	16.3		811	24.5		299	19.9		5239	17.4		6588	18.2	
50+	10	6.8		59	8.2		202	6.1		95	6.3		2655	8.8		3050	8.4	
Age at menopause (y)																		
<40	29	22.7		49	7.1		493	16.8		144	10.8		2512	9.0		3276	9.8	
40–49	51	39.8		265	38.5		1192	40.7		550	41.2		10,883	38.8		13,107	39.1	
50+	48	37.5		375	54.4		1244	42.5		640	48.0		14,650	52.2		17,126	51.1	
Bilateral oophorectomy																		
No	107	73.8		571	80.3		2404	77.6		1224	84.5		24,070	81.4		28,705	81.1	
Yes	38	26.2		140	19.7		692	22.4		225	15.5		5514	18.6		6696	18.9	
Ever pregnant																		
No	*	*		87	12.0		238	7.2		109	7.3		2418	8.0		2894	8.0	
Yes	146	98.0		635	88.0		3061	92.8		1391	92.7		27,697	92.0		33,323	92.0	
Age at first birth (y)[c]																		
Never had term pregnancy	*	*		16	2.9		187	7.3		34	3.1		599	2.3		846	2.8	
<20	45	34.9		47	8.5		911	35.6		282	26.0		4111	16.1		5483	18.1	
20–29	72	55.8		400	72.3		1282	50.2		674	62.2		18,777	73.5		21,421	70.9	
30+	10	7.8		90	16.3		176	6.9		93	8.6		2064	8.1		2466	8.2	
Number of live births																		
Never pregnant	*	*		87	12.0		238	7.2		109	7.3		2418	8.1		2894	8.0	
None	*	*		18	2.5		200	6.1		37	2.5		636	2.1		901	2.5	
1	14	9.4		68	9.4		494	15.0		133	8.9		2269	7.6		3028	8.4	
2–4	91	61.1		465	64.4		1770	53.8		884	59.3		19,768	65.8		23,233	64.3	
5+	39	26.2		84	11.6		585	17.8		328	22.0		4937	16.4		6051	16.8	
Number of pregnancies																		
Never pregnant	*	*		87	12.1		238	7.3		109	7.3		2418	8.0		2894	8.0	
1	*	*		47	6.5		315	9.6		93	6.2		1862	6.2		2360	6.5	
2–4	79	53.0		442	61.3		1679	51.2		745	49.9		17,473	58.1		20,627	57.1	
5+	60	40.3		145	20.1		1050	32.0		545	36.5		8318	27.7		10,265	28.4	
Any induced abortions[c]																		
Pregnant, never had abortion	118	90.1		543	90.0		2291	82.3		1048	87.0		24,043	93.2		28,365	91.8	
One or more abortions	13	9.9		60	10.0		494	17.7		157	13.0		1759	6.8		2520	8.2	
Number of months breastfed																		
Never breastfed	62	42.2		278	38.7		1645	50.7		643	43.3		13,857	46.5		16,671	46.5	
1–6	46	31.3		212	29.5		881	27.2		413	27.8		7619	25.5		9293	25.9	
7–12	14	9.5		114	15.9		370	11.4		188	12.7		3438	11.5		4183	11.7	
13–23	11	7.5		66	9.2		198	6.1		132	8.9		2929	9.8		3372	9.4	
24+	14	9.5		49	6.8		150	4.6		109	7.3		1979	6.6		2328	6.5	

(*continued*)

APPENDIX TABLE 9. *Continued*

Age at tubal ligation (y)												
Never had tubal ligation	113	77.4	547	76.2	2470	75.6	1121	75.1	24,713	82.4	29,305	81.3
<30	*	*	25	3.5	145	4.4	70	4.7	759	2.5	1021	2.8
30–34	11	7.5	51	7.1	280	8.6	89	6.0	1498	5.0	1960	5.4
35–39	*	*	71	9.9	258	7.9	141	9.4	1818	6.1	2326	6.5
40–44	*	*	20	2.8	105	3.2	59	4.0	1003	3.3	1204	3.3
45+			*	*	11	0.3	13	0.9	214	0.7	246	0.7
Age last had any menstrual bleeding (y)												
<40	31	25.6	73	10.7	683	24.4	230	18.5	3327	12.9	4401	14.2
40–44	20	16.5	99	14.5	501	17.9	198	16.0	3401	13.2	4276	13.8
45–49	28	23.1	158	23.2	604	21.6	288	23.2	5637	21.9	6807	22.0
50–54	35	28.9	255	37.4	674	24.1	401	32.3	9108	35.4	10,581	34.2
55–59	6	5.0	82	12.0	255	9.1	104	8.4	3233	12.6	3724	12.0
60+	*	*	15	2.2	79	2.8	20	1.6	1010	3.9	1136	3.7
Current health care provider												
No	12	8.1	45	6.3	318	9.8	354	23.9	2061	6.9	2827	7.9
Yes	136	91.9	674	93.7	2914	90.2	1126	76.1	27,870	93.1	33,111	92.1
Mammogram in last 2 y												
No	34	24.8	160	22.9	624	20.2	478	33.7	5812	19.8	7193	20.5
Yes	103	75.2	538	77.1	2470	79.8	941	66.3	23,530	80.2	27,913	79.5
Pap smear in last 3 y												
No	9	15.3	76	17.5	170	14.8	150	22.0	2088	13.8	2529	14.3
Yes	50	84.7	358	82.5	980	85.2	532	78.0	13,077	86.2	15,173	85.7
Total oral contraceptive duration (y)												
Nonuser	74	49.7	406	56.2	1953	58.9	808	53.6	16,361	54.3	19,856	54.7
<5	46	30.9	171	23.7	662	20.0	379	25.1	7400	24.5	8761	24.1
5–<10	16	10.7	73	10.1	350	10.6	178	11.8	3259	10.8	3914	10.8
10+	13	8.7	72	10.0	352	10.6	142	9.4	3133	10.4	3751	10.3
History of PHT use[d]												
Never	72	48.3	328	45.4	1979	59.8	796	52.9	13,771	45.7	17,160	47.4
Past	35	23.5	107	14.8	556	16.8	238	15.8	5110	17.0	6124	16.9
Current	42	28.2	287	39.8	775	23.4	470	31.3	11,240	37.3	12,956	35.8
Total PHT duration (y)[d]												
Nonuser	72	48.3	328	45.4	1979	59.7	796	52.8	13,771	45.7	17,160	47.3
<5	28	18.8	175	24.2	748	22.6	384	25.5	7067	23.4	8502	23.4
5–<10	20	13.4	103	14.3	261	7.9	155	10.3	3710	12.3	4290	11.8
10–<15	13	8.7	53	7.3	152	4.6	76	5.0	2521	8.4	2846	7.8
15+	16	10.7	63	8.7	177	5.3	96	6.4	3084	10.2	3484	9.6
History of E-alone use[d]												
Never	90	60.4	497	68.8	2256	68.2	1030	68.5	19,735	65.5	23,909	66.0
Past	31	20.8	82	11.4	464	14.0	168	11.2	4111	13.6	4915	13.6
Current	28	18.8	143	19.8	590	17.8	306	20.3	6286	20.9	7427	20.5
Total E-alone duration (y)[d]												
Nonuser	90	60.4	497	68.8	2256	68.0	1030	68.3	19,735	65.4	23,909	65.9
<5	22	14.8	92	12.7	592	17.8	236	15.7	4407	14.6	5402	14.9
5–<10	13	8.7	52	7.2	199	6.0	107	7.1	2004	6.6	2396	6.6
10–<15	9	6.0	28	3.9	127	3.8	55	3.6	1540	5.1	1777	4.9
15+	15	10.1	53	7.3	143	4.3	79	5.2	2467	8.2	2798	7.7

History of E + P use[d]																
Never	124	83.2		518	71.7		2962	89.3		1229	81.6		22,441	74.5		27,606	76.1	
Past	10	6.7		60	8.3		165	5.0		110	7.3		2624	8.7		3003	8.3	
Current	15	10.1		144	19.9		190	5.7		168	11.1		5066	16.8		5651	15.6	
Total E + P duration (y)[d]																		
Nonuser	124	83.2		518	71.7		2962	89.3		1229	81.6		22,441	74.4		27,606	76.1	
<5	13	8.7		115	15.9		221	6.7		192	12.7		4249	14.1		4851	13.4	
5–<10	7	4.7		58	8.0		81	2.4		50	3.3		2075	6.9		2295	6.3	
10–<15	*	*		24	3.3		35	1.1		24	1.6		972	3.2		1072	3.0	
15+	*	*		7	1.0		18	0.5		12	0.8		416	1.4		458	1.3	
Family history of MI																		
No	63	45.7		426	62.6		1700	56.5		811	57.6		13,384	46.5		16,585	48.2	
Yes	75	54.3		254	37.4		1311	43.5		597	42.4		15,413	53.5		17,850	51.8	
Family history of breast cancer																		
No	107	77.5		607	87.3		2591	84.5		1263	88.3		23,424	81.8		28,326	82.4	
Yes	31	22.5		88	12.7		476	15.5		168	11.7		5208	18.2		6043	17.6	
Family history of colorectal cancer																		
No	108	80.0		564	83.7		2392	83.9		1214	89.5		23,196	83.5		27,806	83.8	
Yes	27	20.0		110	16.3		458	16.1		142	10.5		4598	16.5		5388	16.2	
Family history of stroke																		
No	80	58.0		392	57.3		1843	59.8		927	66.5		17,867	62.5		21,367	62.4	
Yes	58	42.0		292	42.7		1237	40.2		466	33.5		10,703	37.5		12,893	37.6	
Family history of adult diabetes																		
No	66	48.2		401	59.4		1424	47.9		727	51.5		19,629	68.1		22,506	65.4	
Yes	71	51.8		274	40.6		1550	52.1		684	48.5		9211	31.9		11,923	34.6	
Parent broke bone after age 40																		
No	87	66.9		460	67.7		2257	79.9		937	68.5		15,951	56.8		19,955	59.6	
Yes	43	33.1		219	32.3		568	20.1		430	31.5		12,155	43.2		13,527	40.4	
Systolic blood pressure (mm Hg)	3317		131.9 ± 16.9	1507		125.7 ± 16.5	149		129.1 ± 16.6	722		129.5 ± 18.2	30,153		127.0 ± 17.1	36,282		127.5 ± 17.2
≤120	45	30.2		236	32.7		917	27.6		644	42.7		11,611	38.5		13,592	37.5	
>120–140	72	48.3		313	43.4		1481	44.6		615	40.8		12,621	41.9		15,270	42.1	
>140	32	21.5		173	24.0		919	27.7		248	16.5		5921	19.6		7420	20.5	
Diastolic blood pressure (mm Hg)	3317		78.7 ± 9.4	1507		75.6 ± 8.9	149		76.1 ± 9.6	722		79.0 ± 9.1	30,147		75.5 ± 8.9	36,276		75.9 ± 9.1
<90	136	91.3		627	86.8		2850	85.9		1410	93.6		28,182	93.5		33,585	92.6	
≥90	13	8.7		95	13.2		467	14.1		97	6.4		1965	6.5		2691	7.4	
History of hypertension																		
Never hypertensive	81	60.0		455	64.4		1422	46.6		992	72.5		18,598	68.8		21,773	66.6	
Untreated hypertensive	11	8.1		49	6.9		318	10.4		123	9.0		2107	7.8		2644	8.1	
Treated hypertensive	43	31.9		203	28.7		1313	43.0		253	18.5		6331	23.4		8279	25.3	
Treated diabetes (pills or shots)																		
No	136	91.9		679	94.0		2943	88.8		1411	93.7		29,112	96.6		34,685	95.6	
Yes	12	8.1		43	6.0		371	11.2		95	6.3		1031	3.4		1581	4.4	
Treated hypercholesterolemia (pills)																		
No	119	88.8		569	81.1		2589	85.7		1186	88.6		23,750	88.2		28,549	87.8	
Yes	15	11.2		133	18.9		432	14.3		153	11.4		3178	11.8		3972	12.2	
Depression (shortened CES-D/DIS ≥ 0.06)																		
No	120	82.8		661	92.7		2723	87.1		1111	81.3		26,713	90.4		31,701	89.7	
Yes	25	17.2		52	7.3		403	12.9		256	18.7		2841	9.6		3629	10.3	

(*continued*)

APPENDIX TABLE 9. *Continued*

Benign breast disease												
No	107	78.7	605	85.5	2474	80.5	1142	84.1	21,627	80.0	26,262	80.2
Yes, 1 biopsy	24	17.6	65	9.2	442	14.4	151	11.1	3954	14.6	4700	14.4
Yes, 2+biopsies	5	3.7	38	5.4	159	5.2	65	4.8	1466	5.4	1764	5.4
History of cardiovascular disease[e]												
No	128	86.5	691	96.0	2835	87.0	1390	93.4	27,331	91.5	32,764	91.3
Yes	20	13.5	29	4.0	423	13.0	98	6.6	2524	8.5	3132	8.7
History of MI												
No	143	96.0	718	99.4	3217	97.0	1494	99.1	29,627	98.3	35,628	98.2
Yes	6	4.0	*	*	100	3.0	13	0.9	526	1.7	654	1.8
History of CABG/PTCA												
No	148	99.3	717	99.6	3192	98.4	1478	99.3	29,470	98.8	35,429	98.8
Yes	*	*	*	*	53	1.6	10	0.7	347	1.2	417	1.2
History of CHF												
No	145	97.3	720	99.7	3274	98.7	1496	99.3	30,020	99.6	36,087	99.5
Yes	*	*	*	*	43	1.3	11	0.7	132	0.4	194	0.5
History of angina												
No	139	93.3	706	98.1	3128	94.9	1464	97.5	29,112	96.8	34,963	96.7
Yes	10	6.7	14	1.9	167	5.1	37	2.5	948	3.2	1192	3.3
History of carotid endarterectomy/angioplasty												
No	149	100.0	721	100.0	3233	99.6	1489	100.0	29,766	99.8	35,784	99.8
Yes	0	0.0	0	0.0	13	0.4	0	0.0	55	0.2	68	0.2
History of DVT												
No	145	97.3	719	99.6	3228	97.3	1481	98.3	29,301	97.2	35,300	97.3
Yes	*	*	*	*	89	2.7	26	1.7	843	2.8	973	2.7
History of PE												
No	148	99.3	717	99.4	3285	99.0	1504	99.8	29,952	99.4	36,037	99.3
Yes	*	*	*	*	32	1.0	*	*	194	0.6	237	0.7
History of PAD												
No	146	98.6	720	99.9	3224	97.9	1483	98.7	29,831	99.2	35,829	99.0
Yes	*	*	*	*	70	2.1	20	1.3	254	0.8	350	1.0
History of stroke												
No	147	98.7	716	99.2	3247	97.9	1490	98.9	29,906	99.2	35,934	99.0
Yes	*	*	6	0.8	70	2.1	17	1.1	247	0.8	348	1.0
History of polyp removal												
No	124	91.2	650	92.2	2792	92.5	1289	95.2	24,644	92.0	29,858	92.2
Yes	12	8.8	55	7.8	225	7.5	65	4.8	2148	8.0	2543	7.8
History of fracture at age 55+[f]												
No	110	89.4	509	90.6	2243	92.3	1922	92.0	20,331	85.1	24,418	86.2
Yes	13	10.6	53	9.4	186	7.7	80	8.0	3549	14.9	3916	13.8
History of hip fracture at age 55+[f]												
No	123	100.0	562	100.0	2426	99.9	999	99.7	23,763	99.5	28,208	99.6
Yes	*	*	*	*	3	0.1	3	0.3	117	0.5	126	0.4
Number of falls in last 12 mo												
None	94	67.1	547	77.2	2167	69.5	963	69.2	18,344	66.1	22,393	66.8
1	28	20.0	118	16.6	564	18.1	260	18.7	5757	20.7	6807	20.3
2	11	7.9	34	4.8	271	8.7	105	7.5	2434	8.8	2888	8.6
3+	7	5.0	10	1.4	116	3.7	64	4.6	1218	4.4	1433	4.3

History of cancer[g]																			
No	144	96.6		694	96.8		3156	96.5		1452	97.4		28,659	95.8		34,512	96.0		
Yes	5	3.4		23	3.2		116	3.5		39	2.6		1241	4.2		1443	4.0		
History of colorectal cancer																			
No	148	99.3		720	99.7		3316	100.0		1507	100.0		30,112	99.9		36,237	99.9		
Yes	*	*		*	*		*	*		0	0.0		41	0.1		45	0.1		
History of endometrial cancer																			
No	149	100.0		718	99.4		3291	99.2		1499	99.5		29,923	99.2		36,009	99.2		
Yes	0	0.0		*	*		26	0.8		8	0.5		230	0.8		273	0.8		
History of melanoma cancer																			
No	148	99.3		722	100.0		3315	99.9		1504	99.8		29,985	99.4		36,108	99.5		
Yes	*	*		0	0.0		*	*		*	*		167	0.6		273	0.5		
History of cervical cancer																			
No	149	100.0		714	99.6		3235	98.7		1481	99.1		29,522	98.8		35,522	98.9		
Yes	0	0.0		*	*		42	1.3		13	0.9		348	1.2		411	1.1		
History of ovarian cancer																			
No	149	100.0		713	99.4		3260	99.5		1492	99.9		29,768	99.6		35,808	99.6		
Yes	0	0.0		*	*		17	0.5		*	*		107	0.4		129	0.4		
History of lung cancer																			
No	149	100.0		717	100.0		3275	99.9		1493	100.0		29,858	100.0		35,917	100.0		
Yes	0	0.0		0	0.0		*	*		0	0.0		13	0.0		16	0.0		
History of osteoporosis																			
No	137	95.1		690	96.5		3098	96.1		1363	93.5		28,265	94.9		33,949	95.0		
Yes	7	4.9		25	3.5		125	3.9		95	6.5		1504	5.1		1785	5.0		
History of arthritis																			
No arthritis	69	50.4		493	69.1		1625	51.5		904	63.5		16,587	57.9		19,916	57.8		
Rheumatoid arthritis	15	10.9		31	4.3		256	8.1		71	5.0		1071	3.7		1475	4.3		
Other arthritis	53	38.7		189	26.5		1272	40.3		448	31.5		10,966	38.3		13,074	37.9		
Total hip BMD (WHO criteria)																			
Normal							190	67.4		86	58.9		1164	56.6		1440	57.9		
Osteopenic							91	32.3		56	38.4		802	39.0		949	38.2		
Osteoporotic							*	*		*	*		92	4.5		97	3.9		
Hip scan (g/cm^2)	19		0.92 ± 0.18	*		*	282		0.97 ± 0.14	146		0.88 ± 0.14	2058		0.85 ± 0.13	2526		0.86 ± 0.14	
Spine scan (g/cm^2)	19		0.98 ± 0.19	*		*	278		1.06 ± 0.18	144		0.97 ± 0.16	2008		0.97 ± 0.16	2470		0.98 ± 0.16	
Whole body scan (g/cm^2)	19		1.02 ± 0.11	*		*	279		1.07 ± 0.11	146		1.04 ± 0.12	2064		1.01 ± 0.10	2529		1.02 ± 0.11	
Lean body mass + BMC (kg)	18		39.7 ± 5.5	*		*	279		44.5 ± 6.5	145		39.0 ± 5.4	2034		39.9 ± 5.2	2497		40.3 ± 5.6	
Fat body mass (kg)	18		38.4 ± 13.8	*		*	279		40.2 ± 13.2	145		34.6 ± 9.8	2034		33.1 ± 10.5	2497		34.0 ± 11.1	

CABG, coronary bypass surgery; PTCA, angioplasty; WHO, World Health Organization; E+P, estrogen+progestin; E-alone, estrogen alone; BMC, bone mineral content; PHT, postmenopausal hormone therapy; BMD, bone mineral density; E + P, estrogen + progestin; MI, myocardial infarction; CHF, congestive heart failure; DVT, deep vein thrombosis; PE, pulmonary embolism; PAD, peripheral arterial disease.

[a]Total includes those of unknown ethnicity.

[b]Hysterectomy at randomization.

[c]Applies only to participants who have ever been pregnant.

[d]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.

[e]Includes MI, stroke, CHF, angina, carotid endarterectomy/angioplasty, DVT, PE, PAD, and CABG/PTCA.

[f]Applies only to participants age 55 and older.

[g]Excluding nonmelanoma skin cancer.

*Data withheld from cells where N < 5 (<10 where data are sensitive).

APPENDIX TABLE 10. Baseline medical history status of WHI Observational Study participants by race/ethnicity

	Race/Ethnicity																	
	American Indian (*N* = 422)			Asian/Pacific Islander (*N* = 2671)			Black (*N* = 7639)			Hispanic (*N* = 3623)			White (*N* = 78,013)			Total[a] (*N* = 93,676)		
Medical History	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD	*N*	%	Mean ± SD
Hysterectomy[b]																		
No	211	50.0		1745	65.4		3447	45.2		1984	54.8		46,303	59.4		54,443	58.2	
Yes	211	50.0		923	34.6		4187	54.8		1634	45.2		31,651	40.6		39,147	41.8	
Age at hysterectomy (y)																		
Not hysterectomized	211	50.0		1745	65.5		3447	45.3		1984	55.0		46,303	59.5		54,443	58.3	
<40	107	25.4		248	9.3		1888	24.8		651	18.0		9392	12.1		12,459	13.3	
40–49	72	17.1		427	16.0		1733	22.8		702	19.5		13,617	17.5		16,792	18.0	
50+	32	7.6		246	9.2		547	7.2		270	7.5		8532	11.0		9750	10.4	
Age at menopause (y)																		
<40	59	15.6		165	6.4		1175	16.8		373	11.4		6477	8.6		8370	9.3	
40–49	191	50.7		934	36.2		2869	41.0		1421	43.4		29,123	38.7		35,040	39.0	
50+	127	33.7		1480	57.4		2958	42.2		1482	45.2		39,712	52.7		46,373	51.7	
Bilateral oophorectomy																		
No	307	78.3		2091	80.0		5489	76.4		2873	81.9		60,962	79.5		72,717	79.4	
Yes	85	21.7		524	20.0		1692	23.6		637	18.1		15,682	20.5		18,891	20.6	
Ever pregnant																		
No	29	6.9		321	12.0		620	8.2		330	9.2		7940	10.2		9357	10.0	
Yes	389	93.1		2347	88.0		6977	91.8		3258	90.8		69,848	89.8		84,004	90.0	
Age at first birth (y)[c]																		
Never had term pregnancy	11	3.6		86	4.2		462	8.0		106	4.3		1830	2.9		2537	3.4	
<20	92	30.4		127	6.3		1935	33.5		562	22.7		7638	12.1		10,517	14.1	
20–29	171	56.4		1469	72.5		2936	50.8		1536	61.9		47,718	75.5		54,513	72.9	
30+	29	9.6		343	16.9		450	7.8		276	11.1		5998	9.5		7205	9.6	
Number of pregnancies																		
Never pregnant	29	7.0		321	12.1		620	8.2		330	9.2		7940	10.2		9357	10.0	
1	30	7.2		210	7.9		796	10.5		235	6.6		5404	7.0		6780	7.3	
2–4	225	54.1		1715	64.5		3872	51.3		1810	50.6		47,394	61.0		55,779	59.9	
5+	132	31.7		414	15.6		2260	29.9		1200	33.6		16,932	21.8		21,251	22.8	
Number of live births																		
Never pregnant	29	7.0		321	12.1		620	8.2		330	9.3		7940	10.2		9357	10.1	
None	11	2.7		90	3.4		507	6.7		117	3.3		1928	2.5		2697	2.9	
1	47	11.3		254	9.6		1195	15.8		314	8.8		6820	8.8		8779	9.4	
2–4	247	59.5		1765	66.5		3963	52.4		2074	58.4		51,803	66.8		60,674	65.2	
5+	81	19.5		226	8.5		1271	16.8		719	20.2		9042	11.7		11,500	12.4	
Any induced abortions[c]																		
Pregnant, never had abortion	316	91.6		1981	89.2		5257	83.6		2473	87.8		60,466	92.1		71,467	91.1	
One or more abortions	29	8.4		239	10.8		1035	16.4		344	12.2		5203	7.9		6965	8.9	
Number of months breastfed																		
Never breastfed	179	43.7		997	37.8		3873	52.3		1563	44.4		38,218	49.7		45,443	49.3	
1–6	121	29.5		854	32.4		1946	26.3		982	27.9		19,613	25.5		23,868	25.9	
7–12	44	10.7		360	13.7		791	10.7		406	11.5		8521	11.1		10,248	11.1	
13–23	30	7.3		227	8.6		440	5.9		248	7.0		6706	8.7		7762	8.4	
24+	36	8.8		199	7.5		353	4.8		325	9.2		3908	5.1		4900	5.3	

Age at tubal ligation (y)												
Never had tubal ligation	333	80.4	2188	82.3	5898	78.4	2716	76.4	65,069	84.0	77,290	83.2
<30	17	4.1	59	2.2	331	4.4	176	4.9	1703	2.2	2322	2.5
30–34	19	4.6	157	5.9	506	6.7	234	6.6	3445	4.4	4417	4.8
35–39	31	7.5	158	5.9	572	7.6	309	8.7	4203	5.4	5335	5.7
40–44	11	2.7	77	2.9	186	2.5	95	2.7	2471	3.2	2878	3.1
45+	*	*	19	0.7	32	0.4	26	0.7	609	0.8	704	0.8
Age last had any menstrual bleeding (y)												
<40	74	21.0	221	8.8	1546	22.8	558	18.2	8293	11.5	10,836	12.6
40–44	69	19.6	313	12.4	1238	18.3	468	15.2	9385	13.1	11,644	13.6
45–49	78	22.2	552	21.9	1440	21.2	720	23.5	15,348	21.4	18,416	21.5
50–54	99	28.1	1017	40.4	1762	26.0	947	30.8	25,894	36.0	30,134	35.1
55–59	19	5.4	311	12.4	606	8.9	275	9.0	9370	13.0	10,709	12.5
60+	13	3.7	102	4.1	190	2.8	102	3.3	3563	5.0	4023	4.7
Current health care provider												
No	41	9.9	122	4.6	554	7.4	550	15.5	3434	4.4	4794	5.2
Yes	374	90.1	2536	95.4	6911	92.6	2994	84.5	73,943	95.6	87,957	94.8
Mammogram in last 2 y												
No	84	21.2	403	15.3	1230	17.2	790	23.4	10,004	13.2	12,710	14.0
Yes	312	78.8	2225	84.7	5929	82.8	2589	76.6	66,061	86.8	78,162	86.0
Pap smear in last 3 y												
No	29	15.8	185	11.2	358	12.2	282	16.1	3644	8.5	4590	9.2
Yes	155	84.2	1473	88.8	2588	87.8	1473	83.9	39,112	91.5	45,392	90.8
Total oral contraceptive duration (y)												
Nonuser	271	64.2	1757	65.8	4953	64.8	2207	60.9	46,176	59.2	56,232	60.0
<5	86	20.4	554	20.7	1346	17.6	831	22.9	17,815	22.8	20,900	22.3
5–<10	37	8.8	190	7.1	699	9.2	321	8.9	7056	9.0	8391	9.0
10+	28	6.6	170	6.4	641	8.4	264	7.3	6966	8.9	8153	8.7
History of PHT use[d]												
Never	204	48.3	929	34.8	4399	57.7	1714	47.5	29,979	38.5	37,817	40.4
Past	50	11.8	349	13.1	1006	13.2	392	10.9	11,137	14.3	13,132	14.0
Current	168	39.8	1391	52.1	2220	29.1	1506	41.7	36,779	47.2	42,579	45.5
Total PHT duration (y)[d]												
Nonuser	204	48.3	929	34.8	4399	57.6	1714	47.3	29,979	38.4	37,817	40.4
<5	77	18.2	665	24.9	1582	20.7	879	24.3	17,337	22.2	20,831	22.2
5–<10	49	11.6	437	16.4	640	8.4	379	10.5	11,003	14.1	12,644	13.5
10–<15	30	7.1	284	10.6	414	5.4	284	7.8	8163	10.5	9287	9.9
15+	62	14.7	356	13.3	604	7.9	367	10.1	11,529	14.8	13,095	14.0
History of E-alone use[d]												
Never	252	59.7	1747	65.4	5111	67.0	2344	64.9	48,051	61.7	58,344	62.4
Past	50	11.8	270	10.1	839	11.0	316	8.7	9440	12.1	11,085	11.8
Current	120	28.4	653	24.5	1677	22.0	954	26.4	20,421	26.2	24,122	25.8
Total E-alone duration (y)[d]												
Nonuser	252	59.7	1747	65.4	5111	66.9	2344	64.7	48,051	61.6	58,344	62.3
<5	61	14.5	338	12.7	1180	15.4	541	14.9	10,362	13.3	12,664	13.5
5–<10	35	8.3	184	6.9	483	6.3	255	7.0	5954	7.6	6989	7.5
10–<15	21	5.0	131	4.9	330	4.3	186	5.1	4610	5.9	5346	5.7
15+	53	12.6	271	10.1	535	7.0	297	8.2	9035	11.6	10,332	11.0
History of E + P use[d]												
Never	356	84.4	1712	64.1	6728	88.1	2867	79.2	54,439	69.8	67,090	71.7
Past	18	4.3	209	7.8	350	4.6	188	5.2	6772	8.7	7632	8.2
Current	48	11.4	749	28.1	558	7.3	566	15.6	16,762	21.5	18,907	20.2

(*continued*)

APPENDIX TABLE 10. *Continued*

Total E + P duration (y)[d]																
Nonuser	356	84.4		1712	64.1		6728	88.1		2867	79.1		54,439	69.8		67,090	71.6	
<5	30	7.1		454	17.0		583	7.6		453	12.5		11,677	15.0		13,370	14.3	
5–<10	18	4.3		284	10.6		192	2.5		142	3.9		6490	8.3		7197	7.7	
10–<15	12	2.8		152	5.7		86	1.1		95	2.6		3617	4.6		4009	4.3	
15+	6	1.4		69	2.6		50	0.7		66	1.8		1789	2.3		2009	2.1	
Family history of MI																		
No	173	45.8		1632	65.3		3866	56.1		1825	55.1		34,025	45.8		42,088	47.5	
Yes	205	54.2		866	34.7		3026	43.9		1488	44.9		40,344	54.2		46,569	52.5	
Family history of breast cancer																		
No	319	83.3		2199	86.2		5867	83.9		2916	87.2		59,082	79.8		71,342	80.6	
Yes	64	16.7		353	13.8		1129	16.1		429	12.8		14,911	20.2		17,130	19.4	
Family history of colorectal cancer																		
No	298	83.7		2035	82.7		5382	83.2		2791	87.7		59,690	83.1		71,161	83.2	
Yes	58	16.3		426	17.3		1090	16.8		393	12.3		12,158	16.9		14,319	16.8	
Family history of stroke																		
No	248	65.3		1467	57.9		4227	60.2		2194	66.3		45,539	61.6		54,401	61.6	
Yes	132	34.7		1066	42.1		2800	39.8		1115	33.7		28,366	38.4		33,959	38.4	
Family history of adult diabetes																		
No	205	55.3		1503	61.1		3319	49.0		1772	53.2		51,921	69.5		59,473	66.9	
Yes	166	44.7		958	38.9		3459	51.0		1558	46.8		22,815	30.5		29,403	33.1	
Parent broke bone after age 40																		
No	240	66.9		1668	68.4		5153	79.9		2186	68.6		42,137	57.8		52,173	60.3	
Yes	119	33.1		769	31.6		1296	20.1		1000	31.4		30,772	42.2		34,340	39.7	
Systolic blood pressure (mm Hg)	422		127.9 ± 17.8	2667		130.0 ± 19.1	7635		132.3 ± 18.4	3619		125.5 ± 17.2	77,904		126.4 ± 17.8	93,551		127.0 ± 18.0
≤120	160	37.9		886	33.2		2161	28.3		1589	43.9		31,914	41.0		37,187	39.8	
>120–140	170	40.3		1058	39.7		3333	43.7		1383	38.2		30,928	39.7		37,389	40.0	
>140	92	21.8		723	27.1		2141	28.0		647	17.9		15,062	19.3		18,975	20.3	
Diastolic blood pressure (mm Hg)	421		75.2 ± 9.2	2670		77.7 ± 9.7	7629		78.0 ± 9.8	3619		74.8 ± 9.2	77,890		74.3 ± 9.2	93,531		74.7 ± 9.4
<90	391	92.9		2348	87.9		6655	87.2		3390	93.7		73,590	94.5		87,549	93.6	
≥90	30	7.1		322	12.1		974	12.8		229	6.3		4300	5.5		5982	6.4	
History of hypertension																		
Never hypertensive	237	57.4		1705	64.5		3317	44.4		2409	69.6		52,709	68.7		61,199	66.5	
Untreated hypertensive	54	13.1		230	8.7		688	9.2		310	9.0		5926	7.7		7318	8.0	
Treated hypertensive	122	29.5		709	26.8		3469	46.4		744	21.5		18,078	23.6		23,464	25.5	
Treated diabetes (pills or shots)																		
No	350	84.3		2528	94.7		6671	87.5		3347	92.6		75,534	96.9		89,654	95.8	
Yes	65	15.7		141	5.3		950	12.5		269	7.4		2406	3.1		3902	4.2	
Treated hypercholesterolemia (pills)																		
No	346	84.0		2072	78.8		6159	82.8		2831	83.1		65,375	85.5		77,835	85.0	
Yes	66	16.0		558	21.2		1277	17.2		576	16.9		11,078	14.5		13,774	15.0	
Depression (shortened CES-D/DIS ⩾ 0.06)																		
No	309	77.3		2431	93.0		6118	85.0		2546	77.4		68,286	89.4		80,758	88.6	
Yes	91	22.8		182	7.0		1082	15.0		743	22.6		8089	10.6		10,368	11.4	
Benign breast disease																		
No	313	80.7		2097	81.7		5548	78.9		2736	82.5		55,649	77.0		67,309	77.5	
Yes, 1 biopsy	54	13.9		349	13.6		1055	15.0		397	12.0		11,471	15.9		13,503	15.6	
Yes, 2+ biopsies	21	5.4		121	4.7		432	6.1		183	5.5		5170	7.2		6001	6.9	

History of cardiovascular disease[e]												
No	322	79.3	2478	93.8	6210	83.2	3123	88.8	67,816	88.1	81,030	87.8
Yes	84	20.7	164	6.2	1250	16.8	395	11.2	9197	11.9	11,279	12.2
History of MI												
No	397	94.1	2631	98.6	7303	95.8	3562	98.3	76,141	97.7	91,283	97.5
Yes	25	5.9	37	1.4	321	4.2	60	1.7	1816	2.3	2306	2.5
History of CABG/PTCA												
No	392	97.3	2598	98.3	7264	97.8	3458	98.7	75,434	98.1	90,393	98.1
Yes	11	2.7	46	1.7	164	2.2	46	1.3	1481	1.9	1773	1.9
History of CHF												
No	413	97.9	2658	99.5	7481	97.9	3576	98.7	77,360	99.2	92,778	99.0
Yes	9	2.1	13	0.5	157	2.1	47	1.3	652	0.8	892	1.0
History of angina												
No	382	92.0	2594	97.3	7047	93.0	3434	95.8	74,172	95.5	88,863	95.3
Yes	33	8.0	73	2.7	529	7.0	150	4.2	3523	4.5	4372	4.7
History of carotid endarterectomy/angioplasty												
No	402	99.8	2643	100.0	7399	99.6	3491	99.6	76,627	99.6	91,826	99.6
Yes	*	*	*	*	29	0.4	13	0.4	292	0.4	344	0.4
History of DVT												
No	395	94.0	2645	99.1	7355	96.4	3529	97.5	74,862	96.0	90,021	96.2
Yes	25	6.0	23	0.9	274	3.6	90	2.5	3096	4.0	3572	3.8
History of PE												
No	414	98.3	2664	99.9	7537	98.8	3592	99.3	77,169	99.0	92,660	99.0
Yes	7	1.7	*	*	95	1.2	26	0.7	810	1.0	959	1.0
History of PAD												
No	401	97.6	2652	99.4	7365	97.2	3514	98.2	76,549	98.5	91,740	98.4
Yes	10	2.4	16	0.6	211	2.8	64	1.8	1131	1.5	1467	1.6
History of stroke												
No	407	96.7	2630	98.5	7392	96.8	3551	98.1	76,966	98.7	92,206	98.5
Yes	14	3.3	39	1.5	243	3.2	70	1.9	1015	1.3	1415	1.5
History of polyp removal												
No	371	90.9	2332	89.0	6721	91.1	3164	92.8	68,005	89.8	81,726	90.0
Yes	37	9.1	287	11.0	653	8.9	244	7.2	7757	10.2	9110	10.0
History of fracture at age 55+[f]												
No	265	86.3	2025	88.7	5672	91.8	2333	89.0	56,150	83.3	67,426	84.3
Yes	42	13.7	257	11.3	506	8.2	289	11.0	11,291	16.7	12,541	15.7
History of hip fracture at age 55+[f]												
No	307	100.0	2276	99.7	6160	99.7	2606	99.4	66,950	99.3	79,429	99.3
Yes	*	*	6	0.3	18	0.3	16	0.6	491	0.7	538	0.7
Number of falls in last 12 mo												
None	252	60.4	2019	76.1	5322	70.6	2363	67.7	51,754	67.1	62,610	67.7
1	90	21.6	430	16.2	1334	17.7	661	18.9	15,658	20.3	18,394	19.9
2	41	9.8	151	5.7	567	7.5	290	8.3	6418	8.3	7579	8.2
3+	34	8.2	53	2.0	312	4.1	175	5.0	3282	4.3	3911	4.2
History of cancer[g]												
No	358	86.5	2453	92.1	6643	87.8	3225	90.7	67,030	86.6	80,853	87.0
Yes	56	13.5	210	7.9	919	12.2	332	9.3	10,413	13.4	12,075	13.0
History of breast cancer												
No	401	95.7	2596	97.3	7171	94.1	3493	96.7	73,630	94.5	88,532	94.6
Yes	18	4.3	73	2.7	449	5.9	119	3.3	4301	5.5	5021	5.4
History of colorectal cancer												
No	416	99.3	2655	99.6	7488	98.7	3579	99.2	77,144	99.1	92,562	99.1
Yes	*	*	11	0.4	98	1.3	29	0.8	701	0.9	860	0.9
History of endometrial cancer												
No	415	98.6	2642	99.0	7506	98.5	3551	98.1	76,443	98.1	91,830	98.2
Yes	6	1.4	26	1.0	111	1.5	69	1.9	1486	1.9	1721	1.8

(*continued*)

APPENDIX TABLE 10. *Continued*

History of melanoma cancer																		
No	415	98.8		2662	99.8		7595	99.8		3583	99.3		76,200	98.0		91,706	98.2	
Yes	5	1.2		5	0.2		16	0.2		25	0.7		1588	2.0		1659	1.8	
History of cervical cancer																		
No	405	98.5		2629	98.8		7427	98.5		3506	98.6		76,318	98.7		91,559	98.7	
Yes	6	1.5		31	1.2		113	1.5		49	1.4		990	1.3		1205	1.3	
History of ovarian cancer																		
No	404	98.1		2645	99.4		7479	99.2		3526	99.1		76,785	99.3		92,119	99.3	
Yes	8	1.9		15	0.6		58	0.8		31	0.9		522	0.7		644	0.7	
History of lung cancer																		
No	409	99.3		2657	99.9		7525	99.7		3550	99.9		77,110	99.8		92,541	99.8	
Yes	*	*		*	*		19	0.3		5	0.1		188	0.2		219	0.2	
History of osteoporosis																		
No	379	91.5		2398	90.8		7097	94.9		3194	91.4		69,924	90.7		84,158	91.0	
Yes	35	8.5		243	9.2		384	5.1		302	8.6		7203	9.3		8282	9.0	
History of arthritis																		
No arthritis	187	45.5		1718	65.2		3486	46.9		1962	56.6		39,671	51.6		47,687	51.8	
Rheumatoid arthritis	38	9.2		123	4.7		696	9.4		263	7.6		3763	4.9		4975	5.4	
Other arthritis	186	45.3		795	30.2		3243	43.7		1241	35.8		33,428	43.5		39,413	42.8	
Total hip BMD (WHO criteria)																		
Normal							490	59.2		227	48.9		2519	50.9		3236	51.9	
Osteopenic							295	35.6		187	40.3		2090	42.2		2572	41.2	
Osteoporotic							43	5.2		50	10.8		338	6.8		431	6.9	
Hip scan (g/cm^2)	108		0.87 ± 0.15	25		0.82 ± 0.14	828		0.93 ± 0.15	464		0.83 ± 0.13	4947		0.83 ± 0.13	6418		0.84 ± 0.14
Spine scan (g/cm^2)	108		0.99 ± 0.17	25		0.95 ± 0.19	826		1.04 ± 0.18	458		0.95 ± 0.16	4849		0.97 ± 0.17	6312		0.98 ± 0.17
Whole body scan (g/cm^2)	107		1.01 ± 0.12	25		1.02 ± 0.12	828		1.05 ± 0.11	464		1.01 ± 0.11	4947		1.01 ± 0.10	6417		1.01 ± 0.11
Lean body mass + BMC (kg)	107		39.4 ± 5.3	24		35.5 ± 5.9	827		43.0 ± 6.2	463		37.9 ± 5.3	4905		39.0 ± 5.3	6371		39.4 ± 5.6
Fat body mass (kg)	107		36.5 ± 11.6	24		19.2 ± 10.2	827		36.7 ± 12.4	463		31.5 ± 10.8	4905		30.5 ± 11.2	6371		31.4 ± 11.6

CABG, coronary bypass surgery; PTCA, angioplasty; WHO, World Health Organization; E + P, estrogen + progestin; E-alone, estrogen alone; BMC, bone mineral content; PHT, postmenopausal hormone therapy; BMD, bone mineral density; MI, myocardial infarction; CHF, congestive heart failure; DVT, deep vein thrombosis; PE, pulmonary embolism; PAD, peripheral arterial disease.

[a]Total includes those of unknown ethnicity.

[b]Hysterectomy at randomization.

[c]Applies only to participants who have ever been pregnant.

[d]Based on estrogen and progesterone pills and patches only (creams and shots excluded). Episodes less than 3 months are excluded.

[e]Includes MI, stroke, CHF, angina, carotid endarterectomy/angioplasty, DVT, PE, PAD, and CABG/PTCA.

[f]Applies only to participants age 55 and older.

[g]Excluding nonmelanoma skin cancer.

*Data withheld from cells where N < 5 (<10 where data are sensitive).

APPENDIX TABLE 11. Baseline dietary intake of WHI Estrogen + Progestin participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 53)		Asian/Pacific Islander (*N* = 342)		Black (*N* = 1045)		Hispanic (*N* = 808)		White (*N* = 13,581)		Total[a] (*N* = 16,049)	
Nutrient[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Energy (kcal)	53	1498 ± 680	342	1360 ± 547	1045	1499 ± 676	808	1515 ± 671	13,581	1562 ± 579	16,049	1550 ± 593
Total fat (gm)	53	62 ± 34	342	48 ± 26	1045	58 ± 33	808	58 ± 32	13,581	57 ± 29	16,049	57 ± 29
Energy from fat (%)	53	37 ± 9	342	32 ± 8	1045	35 ± 9	808	34 ± 8	13,581	33 ± 9	16,049	33 ± 9
Total carbohydrate (gm)	53	171 ± 81	342	172 ± 68	1045	180 ± 81	808	182 ± 81	13,581	185 ± 71	16,049	184 ± 73
Energy from carbohydrates (%)	53	46 ± 10	342	51 ± 9	1045	48 ± 9	808	48 ± 9	13,581	47 ± 9	16,049	48 ± 9
Protein (gm)	53	57 ± 28	342	55 ± 23	1045	57 ± 28	808	61 ± 30	13,581	65 ± 26	16,049	64 ± 26
Energy from protein (%)	53	15 ± 3	342	16 ± 3	1045	15 ± 3	808	16 ± 3	13,581	17 ± 3	16,049	16 ± 3
Alcohol (gm)	53	0.9 ± 0.8	342	0.5 ± 0.5	1045	0.8 ± 0.7	808	0.8 ± 0.7	13,581	2.1 ± 2.6	16,049	1.9 ± 2.2
Energy from alcohol (%)	53	0.5 ± 0.3	342	0.4 ± 0.2	1045	0.5 ± 0.3	808	0.5 ± 0.3	13,581	1.2 ± 1.1	16,049	1.1 ± 1
Total PFA (gm)	53	13 ± 7	342	11 ± 6	1045	13 ± 7	808	12 ± 7	13,581	12 ± 6	16,049	12 ± 6
Total MFA (gm)	53	23 ± 12	342	18 ± 9	1045	22 ± 12	808	21 ± 12	13,581	21 ± 11	16,049	21 ± 11
Total SFA (gm)	53	21 ± 13	342	15 ± 8	1045	19 ± 11	808	19 ± 11	13,581	20 ± 10	16,049	20 ± 10
Energy from SFA (%)	53	13 ± 4	342	10 ± 3	1045	11 ± 3	808	11 ± 3	13,581	11 ± 3	16,049	11 ± 3
Total trans fatty acid (gm)	53	3.8 ± 2.1	342	2.6 ± 1.1	1045	4 ± 2.1	808	3.1 ± 1.5	13,581	3.5 ± 1.7	16,049	3.5 ± 1.7
Animal protein (gm)	53	38 ± 23	342	34 ± 17	1045	39 ± 22	808	42 ± 23	13,581	45 ± 21	16,049	44 ± 21
Vegetable protein (gm)	53	17 ± 8	342	19 ± 8	1045	16 ± 8	808	17 ± 8	13,581	18 ± 7	16,049	18 ± 7
Dietary fiber (gm)	53	13 ± 6	342	13 ± 5	1045	13 ± 6	808	14 ± 6	13,581	15 ± 6	16,049	15 ± 6
Water soluble fiber (gm)	53	4.5 ± 1.7	342	4.8 ± 1.7	1045	4.7 ± 1.8	808	4.7 ± 1.8	13,581	5.3 ± 1.8	16,049	5.2 ± 1.8
Insoluble dietary fiber (gm)	53	9 ± 4	342	8 ± 3	1045	9 ± 4	808	9 ± 4	13,581	10 ± 4	16,049	10 ± 4
Cholesterol (mg)	53	210 ± 145	342	177 ± 100	1045	203 ± 131	808	205 ± 132	13,581	193 ± 107	16,049	194 ± 110
Total vitamin A (mcg Re)	53	6140 ± 3774	342	7777 ± 4390	1045	7617 ± 4834	808	5926 ± 3836	13,581	7856 ± 4149	16,049	7721 ± 4227
Vitamin D (mcg)	53	4.1 ± 2	342	3.5 ± 1.6	1045	3.9 ± 1.9	808	3.6 ± 1.9	13,581	4.6 ± 2.2	16,049	4.5 ± 2.1
Total alpha-toc eq (mg)	53	7.4 ± 3	342	7.2 ± 3	1045	7.8 ± 3.4	808	7.2 ± 3.2	13,581	7.9 ± 3.2	16,049	7.8 ± 3.2
Vitamin K (NDS value) (mg)	53	81 ± 42	342	94 ± 49	1045	94 ± 52	808	68 ± 36	13,581	79 ± 38	16,049	80 ± 39
Vitamin C (mg)	53	67 ± 43	342	84 ± 50	1045	89 ± 54	808	78 ± 50	13,581	91 ± 51	16,049	90 ± 51
Thiamin (mg)	53	1.2 ± 0.3	342	1.2 ± 0.3	1045	1.2 ± 0.3	808	1.2 ± 0.3	13,581	1.3 ± 0.3	16,049	1.3 ± 0.3
Riboflavin (mg)	53	1.5 ± 0.4	342	1.2 ± 0.3	1045	1.4 ± 0.4	808	1.5 ± 0.4	13,581	1.7 ± 0.4	16,049	1.6 ± 0.4
Niacin (mg)	53	15 ± 6	342	15 ± 6	1045	15 ± 7	808	15 ± 7	13,581	17 ± 6	16,049	17 ± 6
Vitamin B_6 (mg)	53	1.4 ± 0.4	342	1.4 ± 0.3	1045	1.4 ± 0.4	808	1.4 ± 0.4	13,581	1.6 ± 0.4	16,049	1.6 ± 0.4
Folacin (mcg)	53	192 ± 83	342	192 ± 82	1045	204 ± 97	808	186 ± 90	13,581	231 ± 94	16,049	225 ± 95
Vitamin B_{12} (mcg)	53	4.2 ± 2.2	342	4.6 ± 2.4	1045	5.5 ± 3.4	808	4.5 ± 2.5	13,581	4.9 ± 2.2	16,049	4.9 ± 2.3
Calcium (mg)	53	567 ± 340	342	455 ± 241	1045	511 ± 304	808	629 ± 362	13,581	706 ± 363	16,049	679 ± 363
Total calcium (mg)	53	687 ± 448	342	728 ± 490	1045	623 ± 412	808	771 ± 498	13,581	962 ± 558	16,049	917 ± 555
Magnesium (mg)	53	212 ± 95	342	210 ± 82	1045	211 ± 95	808	216 ± 96	13,581	252 ± 93	16,049	246 ± 94
Iron (mg)	53	11 ± 5	342	11 ± 4	1045	11 ± 5	808	11 ± 5	13,581	13 ± 5	16,049	12 ± 5
Zinc (mg)	53	9 ± 4	342	8 ± 3	1045	9 ± 4	808	9 ± 4	13,581	10 ± 4	16,049	10 ± 4
Sodium (mg)	53	2417 ± 1114	342	2294 ± 1001	1045	2379 ± 1175	808	2372 ± 1184	13,581	2564 ± 1020	16,049	2535 ± 1047
Potassium (mg)	53	2087 ± 893	342	2032 ± 802	1045	2065 ± 937	808	2127 ± 957	13,581	2535 ± 922	16,049	2464 ± 943
Phosphorous (mg)	53	905 ± 463	342	829 ± 351	1045	877 ± 435	808	978 ± 475	13,581	1066 ± 441	16,049	1041 ± 447
Copper (mg)	53	1 ± 0.2	342	1 ± 0.2	1045	1 ± 0.2	808	1 ± 0.2	13,581	1.1 ± 0.2	16,049	1.1 ± 0.2
Total carotenoids (mcg)	53	11,628 ± 6738	342	11,612 ± 6286	1045	10,646 ± 6526	808	9998 ± 6544	13,581	12,416 ± 6514	16,049	12,133 ± 6577
Alpha-carotene (mcg)	53	503 ± 498	342	795 ± 585	1045	518 ± 492	808	490 ± 464	13,581	756 ± 591	16,049	721 ± 586
Beta-carotene (mcg)	53	2392 ± 1702	342	3460 ± 2194	1045	3040 ± 2184	808	2235 ± 1713	13,581	3089 ± 1938	16,049	3041 ± 1965
Lycopene (mcg)	53	6758 ± 4333	342	4946 ± 3482	1045	4600 ± 3771	808	5324 ± 4526	13,581	6448 ± 4151	16,049	6209 ± 4200
Lutein + zeaxanthin (mcg)	53	1303 ± 778	342	1460 ± 823	1045	1540 ± 944	808	1143 ± 671	13,581	1348 ± 711	16,049	1350 ± 729
Fruits and vegetables (servings/day)	53	2.6 ± 1.2	342	3.2 ± 1.3	1045	3.2 ± 1.5	808	2.6 ± 1.3	13,581	3.6 ± 1.5	16,049	3.5 ± 1.5
Fruits and vegetables (servings/day/1000 kcal)	53	1.8 ± 0.8	342	2.4 ± 0.9	1045	2.2 ± 0.9	808	1.8 ± 0.8	13,581	2.3 ± 0.9	16,049	2.3 ± 0.9
Grains (servings/day)	53	4 ± 1.9	342	4.2 ± 1.7	1045	3.7 ± 1.8	808	4.4 ± 2.2	13,579	4.1 ± 1.7	16,047	4.1 ± 1.7
Grains (servings/day/1000 kcal)	53	2.6 ± 0.7	342	3 ± 0.8	1045	2.4 ± 0.7	808	2.9 ± 0.9	13,579	2.6 ± 0.7	16,047	2.6 ± 0.7

[a]Total includes those of unknown ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 12. Baseline dietary intake of WHI Estrogen-Alone participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 67)		Asian/Pacific Islander (*N* = 152)		Black (N = 1488)		Hispanic (*N* = 611)		White (*N* = 7796)		Total[a] (N = 10,250)	
Nutrient[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Energy (kcal)	67	1577 ± 687	152	1341 ± 607	1488	1463 ± 671	611	1577 ± 730	7796	1529 ± 589	10,250	1517 ± 614
Total fat (gm)	67	59 ± 31	152	48 ± 29	1488	57 ± 32	611	61 ± 35	7796	58 ± 29	10,250	58 ± 30
Energy from fat (%)	67	34 ± 7	152	32 ± 9	1488	35 ± 9	611	35 ± 8	7796	34 ± 9	10,250	34 ± 9
Total carbohydrate (gm)	67	192 ± 77	152	166 ± 72	1488	176 ± 81	611	187 ± 88	7796	179 ± 72	10,250	179 ± 74
Energy from carbohydrates (%)	67	49 ± 9	152	49 ± 10	1488	48 ± 10	611	47 ± 10	7796	47 ± 9	10,250	47 ± 9
Protein (gm)	67	64 ± 33	152	56 ± 27	1488	57 ± 28	611	63 ± 31	7796	63 ± 26	10,250	62 ± 27
Energy from protein (%)	67	16 ± 4	152	17 ± 3	1488	16 ± 3	611	16 ± 3	7796	17 ± 3	10,250	16 ± 3
Alcohol (gm)	67	1 ± 1.1	152	0.4 ± 0.3	1488	0.6 ± 0.6	611	0.6 ± 0.6	7796	1.5 ± 1.7	10,250	1.2 ± 1.4
Energy from alcohol (%)	67	0.5 ± 0.4	152	0.2 ± 0.1	1488	0.4 ± 0.3	611	0.4 ± 0.2	7796	0.9 ± 0.8	10,250	0.8 ± 0.6
Total PFA (gm)	67	12 ± 6	152	11 ± 6	1488	12 ± 7	611	13 ± 7	7796	12 ± 6	10,250	12 ± 6
Total MFA (gm)	67	22 ± 12	152	18 ± 11	1488	21 ± 12	611	23 ± 13	7796	21 ± 11	10,250	21 ± 11
Total SFA (gm)	67	20 ± 11	152	15 ± 9	1488	18 ± 11	611	20 ± 12	7796	20 ± 11	10,250	20 ± 11
Energy from SFA (%)	67	11 ± 3	152	10 ± 3	1488	11 ± 3	611	12 ± 3	7796	12 ± 3	10,250	12 ± 3
Total trans fatty acid (gm)	67	3.5 ± 1.7	152	2.6 ± 1.3	1488	3.9 ± 2.1	611	3.4 ± 1.7	7796	3.7 ± 1.7	10,250	3.6 ± 1.8
Animal protein (gm)	67	44 ± 27	152	36 ± 22	1488	40 ± 23	611	43 ± 25	7796	44 ± 21	10,250	43 ± 22
Vegetable protein (gm)	67	18 ± 8	152	18 ± 8	1488	16 ± 8	611	18 ± 9	7796	18 ± 7	10,250	17 ± 7
Dietary fiber (gm)	67	16 ± 7	152	12 ± 5	1488	13 ± 6	611	14 ± 7	7796	15 ± 6	10,250	14 ± 6
Water soluble fiber (gm)	67	5.5 ± 2.1	152	4.5 ± 1.7	1488	4.5 ± 1.8	611	4.8 ± 1.9	7796	5.1 ± 1.8	10,250	5 ± 1.8
Insoluble dietary fiber (gm)	67	10 ± 4	152	8 ± 3	1488	8 ± 4	611	9 ± 4	7796	10 ± 4	10,250	9 ± 4
Cholesterol (mg)	67	218 ± 136	152	176 ± 117	1488	204 ± 131	611	217 ± 138	7796	197 ± 111	10,250	199 ± 116
Total vitamin A (mcg Re)	67	7745 ± 5162	152	7506 ± 4804	1488	7441 ± 4682	611	6009 ± 3810	7796	7549 ± 4094	10,250	7422 ± 4208
Vitamin D (mcg)	67	4.5 ± 2.4	152	3.7 ± 1.9	1488	3.8 ± 1.9	611	3.7 ± 1.9	7796	4.5 ± 2.2	10,250	4.3 ± 2.1
Total alpha-toc eq (mg)	67	7.7 ± 3.1	152	7.1 ± 3	1488	7.4 ± 3.4	611	7.4 ± 3.3	7796	7.7 ± 3.2	10,250	7.6 ± 3.2
Vitamin K (NDS value) (mg)	67	84 ± 44	152	96 ± 54	1488	90 ± 50	611	70 ± 37	7796	77 ± 37	10,250	79 ± 40
Vitamin C (mg)	67	95 ± 59	152	76 ± 52	1488	85 ± 55	611	78 ± 52	7796	85 ± 49	10,250	85 ± 51
Thiamin (mg)	67	1.3 ± 0.3	152	1.2 ± 0.3	1488	1.2 ± 0.3	611	1.3 ± 0.3	7796	1.3 ± 0.3	10,250	1.3 ± 0.3
Riboflavin (mg)	67	1.7 ± 0.5	152	1.2 ± 0.3	1488	1.4 ± 0.4	611	1.5 ± 0.5	7796	1.6 ± 0.4	10,250	1.6 ± 0.4
Niacin (mg)	67	17 ± 7	152	15 ± 6	1488	15 ± 7	611	15 ± 7	7796	17 ± 6	10,250	16 ± 7
Vitamin B_6 (mg)	67	1.6 ± 0.4	152	1.3 ± 0.4	1488	1.4 ± 0.4	611	1.5 ± 0.4	7796	1.6 ± 0.4	10,250	1.5 ± 0.4
Folacin (mcg)	67	231 ± 94	152	186 ± 87	1488	199 ± 98	611	188 ± 92	7796	221 ± 93	10,250	214 ± 95
Vitamin B_{12} (mcg)	67	5.3 ± 3.2	152	4.6 ± 2.6	1488	5.6 ± 3.4	611	4.6 ± 2.5	7796	4.8 ± 2.2	10,250	4.9 ± 2.4
Calcium (mg)	67	668 ± 384	152	461 ± 281	1488	491 ± 290	611	632 ± 389	7796	664 ± 356	10,250	628 ± 353
Total calcium (mg)	67	809 ± 531	152	687 ± 473	1488	587 ± 384	611	774 ± 510	7796	879 ± 529	10,250	816 ± 516
Magnesium (mg)	67	249 ± 104	152	207 ± 89	1488	205 ± 93	611	223 ± 100	7796	240 ± 93	10,250	233 ± 95
Iron (mg)	67	12 ± 5	152	10 ± 4	1488	11 ± 5	611	11 ± 5	7796	12 ± 5	10,250	12 ± 5
Zinc (mg)	67	10 ± 5	152	8 ± 4	1488	8 ± 4	611	9 ± 4	7796	10 ± 4	10,250	9 ± 4
Sodium (mg)	67	2586 ± 1247	152	2317 ± 1027	1488	2374 ± 1168	611	2468 ± 1229	7796	2527 ± 1031	10,250	2494 ± 1071
Potassium (mg)	67	2530 ± 1085	152	2000 ± 908	1488	1998 ± 916	611	2186 ± 981	7796	2416 ± 923	10,250	2326 ± 946
Phosphorous (mg)	67	1042 ± 535	152	837 ± 412	1488	863 ± 430	611	1007 ± 509	7796	1025 ± 443	10,250	993 ± 450
Copper (mg)	67	1.1 ± 0.3	152	1 ± 0.2	1488	1 ± 0.2	611	1 ± 0.2	7796	1 ± 0.2	10,250	1 ± 0.2
Total carotenoids (mcg)	67	12,410 ± 7676	152	11,042 ± 6084	1488	10,180 ± 6147	611	10,231 ± 6459	7796	11,919 ± 6447	10,250	11,526 ± 6460
Alpha-carotene (mcg)	67	633 ± 540	152	782 ± 614	1488	495 ± 464	611	490 ± 479	7796	707 ± 572	10,250	657 ± 559
Beta-carotene (mcg)	67	3056 ± 2285	152	3319 ± 2333	1488	2962 ± 2100	611	2262 ± 1704	7796	2941 ± 1891	10,250	2902 ± 1930
Lycopene (mcg)	67	6504 ± 4419	152	4575 ± 3140	1488	4311 ± 3544	611	5478 ± 4294	7796	6227 ± 4120	10,250	5828 ± 4124
Lutein + zeaxanthin (mcg)	67	1492 ± 881	152	1480 ± 929	1488	1507 ± 924	611	1199 ± 688	7796	1296 ± 688	10,250	1322 ± 730
Fruits and vegetables (servings/day)	67	3.7 ± 1.7	152	2.9 ± 1.4	1488	3.1 ± 1.4	611	2.6 ± 1.3	7796	3.4 ± 1.5	10,250	3.3 ± 1.5
Fruits and vegetables (servings/day/1000 kcal)	67	2.4 ± 1	152	2.2 ± 1	1488	2.1 ± 0.9	611	1.7 ± 0.8	7796	2.3 ± 0.9	10,250	2.2 ± 0.9
Grains (servings/day)	67	4.1 ± 1.7	152	4.1 ± 1.5	1486	3.7 ± 1.7	611	4.7 ± 2.4	7795	4 ± 1.7	10,247	4 ± 1.7
Grains (servings/day/1000 kcal)	67	2.6 ± 0.7	152	3 ± 0.7	1486	2.5 ± 0.7	611	2.9 ± 0.9	7795	2.6 ± 0.7	10,247	2.6 ± 0.7

[a]Total includes those of unknown ethnicity.

[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 13. Baseline dietary intake of WHI Dietary Modification participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 203)		Asian/Pacific Islander (*N* = 1103)		Black (*N* = 5245)		Hispanic (*N* = 1844)		White (*N* = 39,575)		Total[a] (*N* = 48,614)	
Nutrient[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Energy (kcal)	203	1594 ± 679	1103	1545 ± 614	5245	1570 ± 703	1844	1670 ± 732	39,575	1680 ± 618	48,614	1663 ± 636
Total fat (gm)	203	70 ± 32	1103	65 ± 28	5245	69 ± 33	1844	72 ± 33	39,575	72 ± 29	48,614	71 ± 29
Energy from fat (%)	203	39 ± 5	1103	38 ± 4	5245	40 ± 5	1844	39 ± 5	39,575	39 ± 5	48,614	39 ± 5
Total carbohydrate (gm)	203	175 ± 77	1103	177 ± 70	5245	175 ± 81	1844	187 ± 84	39,575	185 ± 72	48,614	184 ± 73
Energy from carbohydrates (%)	203	44 ± 7	1103	46 ± 6	5245	44 ± 7	1844	45 ± 6	39,575	44 ± 6	48,614	44 ± 6
Protein (gm)	203	63 ± 29	1103	63 ± 27	5245	61 ± 29	1844	67 ± 31	39,575	68 ± 27	48,614	67 ± 27
Energy from protein (%)	203	16 ± 3	1103	16 ± 3	5245	16 ± 3	1844	16 ± 3	39,575	16 ± 3	48,614	16 ± 3
Alcohol (gm)	203	1.3 ± 1.4	1103	0.4 ± 0.3	5245	0.7 ± 0.6	1844	0.9 ± 0.8	39,575	1.9 ± 2.1	48,614	1.6 ± 1.8
Energy from alcohol (%)	203	0.8 ± 0.6	1103	0.3 ± 0.1	5245	0.4 ± 0.2	1844	0.5 ± 0.3	39,575	1 ± 0.8	48,614	0.9 ± 0.7
Total PFA (gm)	203	14 ± 7	1103	15 ± 6	5245	15 ± 7	1844	15 ± 7	39,575	15 ± 6	48,614	15 ± 6
Total MFA (gm)	203	26 ± 12	1103	25 ± 10	5245	26 ± 12	1844	27 ± 13	39,575	27 ± 10	48,614	26 ± 11
Total SFA (gm)	203	24 ± 11	1103	20 ± 9	5245	22 ± 11	1844	24 ± 12	39,575	25 ± 11	48,614	24 ± 11
Energy from SFA (%)	203	13 ± 3	1103	12 ± 2	5245	13 ± 2	1844	13 ± 2	39,575	13 ± 2	48,614	13 ± 2
Total trans fatty acid (gm)	203	4.4 ± 2	1103	3.4 ± 1.4	5245	4.7 ± 2.3	1844	3.9 ± 1.8	39,575	4.4 ± 1.9	48,614	4.4 ± 1.9
Animal protein (gm)	203	43 ± 23	1103	41 ± 21	5245	43 ± 23	1844	47 ± 24	39,575	48 ± 21	48,614	47 ± 22
Vegetable protein (gm)	203	18 ± 8	1103	20 ± 8	5245	17 ± 8	1844	19 ± 9	39,575	19 ± 7	48,614	19 ± 8
Dietary fiber (gm)	203	14 ± 6	1103	13 ± 5	5245	13 ± 6	1844	14 ± 6	39,575	15 ± 6	48,614	15 ± 6
Water soluble fiber (gm)	203	4.9 ± 1.7	1103	4.8 ± 1.7	5245	4.5 ± 1.7	1844	4.8 ± 1.8	39,575	5.2 ± 1.7	48,614	5.1 ± 1.7
Insoluble dietary fiber (gm)	203	9 ± 4	1103	9 ± 3	5245	8 ± 4	1844	9 ± 4	39,575	10 ± 4	48,614	10 ± 4
Cholesterol (mg)	203	229 ± 132	1103	214 ± 114	5245	231 ± 132	1844	242 ± 129	39,575	228 ± 111	48,614	229 ± 114
Total vitamin A (mcg Re)	203	6899 ± 3834	1103	7864 ± 4467	5245	7302 ± 4307	1844	6062 ± 3549	39,575	7686 ± 3785	48,614	7572 ± 3881
Vitamin D (mcg)	203	4.4 ± 2	1103	3.9 ± 1.8	5245	4.1 ± 2	1844	4 ± 1.9	39,575	4.8 ± 2.1	48,614	4.7 ± 2.1
Total alpha-toc eq (mg)	203	8.2 ± 3.5	1103	8.7 ± 3.4	5245	8.4 ± 3.6	1844	8.4 ± 3.5	39,575	8.9 ± 3.5	48,614	8.8 ± 3.5
Vitamin K (NDS value) (mg)	203	84 ± 46	1103	108 ± 55	5245	95 ± 49	1844	74 ± 37	39,575	83 ± 38	48,614	85 ± 40
Vitamin C (mg)	203	74 ± 41	1103	78 ± 45	5245	81 ± 48	1844	76 ± 46	39,575	86 ± 45	48,614	85 ± 46
Thiamin (mg)	203	1.2 ± 0.3	1103	1.3 ± 0.3	5245	1.2 ± 0.3	1844	1.3 ± 0.3	39,575	1.4 ± 0.3	48,614	1.3 ± 0.3
Riboflavin (mg)	203	1.6 ± 0.4	1103	1.3 ± 0.3	5245	1.5 ± 0.4	1844	1.6 ± 0.5	39,575	1.7 ± 0.4	48,614	1.7 ± 0.4
Niacin (mg)	203	16 ± 7	1103	16 ± 7	5245	16 ± 7	1844	17 ± 7	39,575	18 ± 7	48,614	17 ± 7
Vitamin B_6 (mg)	203	1.5 ± 0.4	1103	1.5 ± 0.4	5245	1.4 ± 0.4	1844	1.5 ± 0.4	39,575	1.6 ± 0.4	48,614	1.6 ± 0.4
Folacin (mcg)	203	209 ± 87	1103	197 ± 85	5245	198 ± 93	1844	194 ± 88	39,575	226 ± 89	48,614	221 ± 91
Vitamin B_{12} (mcg)	203	5.1 ± 2.7	1103	5.1 ± 2.6	5245	5.9 ± 3.4	1844	5 ± 2.4	39,575	5.2 ± 2.2	48,614	5.2 ± 2.4
Calcium (mg)	203	621 ± 341	1103	482 ± 253	5245	513 ± 294	1844	660 ± 378	39,575	704 ± 351	48,614	671 ± 351
Total calcium (mg)	203	816 ± 503	1103	797 ± 513	5245	621 ± 394	1844	841 ± 529	39,575	976 ± 555	48,614	918 ± 550
Magnesium (mg)	203	231 ± 92	1103	219 ± 86	5245	209 ± 93	1844	229 ± 99	39,575	250 ± 91	48,614	243 ± 93
Iron (mg)	203	12 ± 5	1103	11 ± 5	5245	11 ± 5	1844	12 ± 5	39,575	13 ± 5	48,614	12 ± 5
Zinc (mg)	203	9 ± 4	1103	9 ± 4	5245	9 ± 4	1844	10 ± 4	39,575	11 ± 4	48,614	10 ± 4
Sodium (mg)	203	2567 ± 1164	1103	2569 ± 1074	5245	2533 ± 1182	1844	2640 ± 1242	39,575	2738 ± 1066	48,614	2705 ± 1094
Potassium (mg)	203	2252 ± 892	1103	2108 ± 858	5245	2006 ± 881	1844	2220 ± 961	39,575	2479 ± 882	48,614	2400 ± 907
Phosphorous (mg)	203	997 ± 460	1103	908 ± 397	5245	907 ± 435	1844	1054 ± 500	39,575	1095 ± 447	48,614	1065 ± 453
Copper (mg)	203	1 ± 0.2	1103	1.1 ± 0.2	5245	1 ± 0.2	1844	1 ± 0.2	39,575	1.1 ± 0.2	48,614	1.1 ± 0.2
Total carotenoids (mcg)	203	11,685 ± 6396	1103	11,745 ± 6267	5245	10,159 ± 5888	1844	10,545 ± 6356	39,575	12,352 ± 6072	48,614	11,998 ± 6147
Alpha-carotene (mcg)	203	568 ± 447	1103	836 ± 613	5245	491 ± 429	1844	501 ± 440	39,575	720 ± 525	48,614	682 ± 523
Beta-carotene (mcg)	203	2641 ± 1706	1103	3467 ± 2181	5245	2863 ± 1909	1844	2282 ± 1589	39,575	2969 ± 1723	48,614	2936 ± 1761
Lycopene (mcg)	203	6386 ± 4334	1103	5077 ± 3657	5245	4492 ± 3489	1844	5882 ± 4338	39,575	6661 ± 4024	48,614	6307 ± 4079
Lutein + zeaxanthin (mcg)	203	1321 ± 741	1103	1479 ± 824	5245	1469 ± 849	1844	1176 ± 638	39,575	1310 ± 638	48,614	1324 ± 668
Fruits and vegetables (servings/day)	203	2.9 ± 1.2	1103	3 ± 1.2	5245	2.9 ± 1.2	1844	2.6 ± 1.1	39,575	3.4 ± 1.3	48,614	3.3 ± 1.3
Fruits and vegetables (servings/day/1000 kcal)	203	1.8 ± 0.6	1103	2 ± 0.7	5245	1.9 ± 0.7	1844	1.6 ± 0.6	39,575	2 ± 0.6	48,614	2 ± 0.7
Grains (servings/day)	203	4 ± 1.8	1103	4.5 ± 1.7	5244	3.9 ± 1.8	1844	4.9 ± 2.4	39,572	4.3 ± 1.7	48,610	4.3 ± 1.8
Grains (servings/day/1000 kcal)	203	2.5 ± 0.7	1103	2.9 ± 0.6	5244	2.4 ± 0.6	1844	2.9 ± 0.8	39,572	2.5 ± 0.6	48,610	2.5 ± 0.6

[a]Total includes those of unknown ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 14. Baseline dietary intake of WHI Calcium and Vitamin D participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 143)		Asian/Pacific Islander (*N* = 704)		Black (*N* = 3190)		Hispanic (*N* = 1436)		White (*N* = 29,693)		Total[a] (*N* = 35,583)	
Nutrient[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Energy (kcal)	143	1569 ± 653	704	1470 ± 614	3190	1543 ± 698	1436	1600 ± 724	29,693	1629 ± 604	35,583	1616 ± 622
Total fat (gm)	143	64 ± 32	704	58 ± 29	3190	64 ± 34	1436	64 ± 34	29,693	66 ± 30	35,583	65 ± 31
Energy from fat (%)	143	37 ± 8	704	35 ± 7	3190	37 ± 7	1436	36 ± 7	29,693	36 ± 7	35,583	36 ± 7
Total carbohydrate (gm)	143	178 ± 76	704	175 ± 72	3190	177 ± 82	1436	187 ± 85	29,693	185 ± 71	35,583	184 ± 73
Energy from carbohydrates (%)	143	45 ± 9	704	48 ± 7	3190	46 ± 8	1436	47 ± 8	29,693	45 ± 8	35,583	46 ± 8
Protein (gm)	143	62 ± 29	704	60 ± 27	3190	60 ± 29	1436	64 ± 31	29,693	67 ± 26	35,583	66 ± 27
Energy from protein (%)	143	16 ± 3	704	16 ± 3	3190	16 ± 3	1436	16 ± 3	29,693	16 ± 3	35,583	16 ± 3
Alcohol (gm)	143	1.3 ± 1.4	704	0.5 ± 0.4	3190	0.7 ± 0.6	1436	0.9 ± 0.8	29,693	2 ± 2.3	35,583	1.7 ± 1.9
Energy from alcohol (%)	143	0.7 ± 0.6	704	0.3 ± 0.2	3190	0.4 ± 0.3	1436	0.5 ± 0.3	29,693	1.1 ± 0.9	35,583	1 ± 0.8
Total PFA (gm)	143	13 ± 6	704	13 ± 7	3190	14 ± 7	1436	13 ± 7	29,693	13 ± 6	35,583	13 ± 6
Total MFA (gm)	143	24 ± 11	704	22 ± 11	3190	24 ± 13	1436	24 ± 13	29,693	24 ± 11	35,583	24 ± 11
Total SFA (gm)	143	22 ± 11	704	18 ± 9	3190	21 ± 11	1436	21 ± 12	29,693	23 ± 11	35,583	22 ± 11
Energy from SFA (%)	143	13 ± 3	704	11 ± 3	3190	12 ± 3	1436	12 ± 3	29,693	13 ± 3	35,583	12 ± 3
Total trans fatty acid (gm)	143	4 ± 1.9	704	3.1 ± 1.4	3190	4.4 ± 2.2	1436	3.6 ± 1.8	29,693	4 ± 1.8	35,583	4 ± 1.8
Animal protein (gm)	143	42 ± 23	704	39 ± 21	3190	42 ± 23	1436	44 ± 24	29,693	47 ± 21	35,583	46 ± 22
Vegetable protein (gm)	143	18 ± 8	704	20 ± 8	3190	17 ± 8	1436	18 ± 9	29,693	19 ± 7	35,583	18 ± 8
Dietary fiber (gm)	143	14 ± 6	704	13 ± 5	3190	13 ± 6	1436	14 ± 7	29,693	15 ± 6	35,583	15 ± 6
Water soluble fiber (gm)	143	5 ± 1.8	704	4.8 ± 1.7	3190	4.6 ± 1.7	1436	4.8 ± 1.9	29,693	5.3 ± 1.7	35,583	5.2 ± 1.7
Insoluble dietary fiber (gm)	143	9 ± 4	704	8 ± 3	3190	8 ± 4	1436	9 ± 4	29,693	10 ± 4	35,583	10 ± 4
Cholesterol (mg)	143	214 ± 132	704	197 ± 113	3190	220 ± 132	1436	221 ± 133	29,693	214 ± 110	35,583	214 ± 114
Total vitamin A (mcg Re)	143	6863 ± 4093	704	7869 ± 4521	3190	7419 ± 4450	1436	6086 ± 3745	29,693	7753 ± 3921	35,583	7641 ± 4009
Vitamin D (mcg)	143	4.3 ± 2.1	704	3.8 ± 1.8	3190	4 ± 1.9	1436	3.8 ± 1.9	29,693	4.7 ± 2.2	35,583	4.6 ± 2.1
Total alpha-toc eq (mg)	143	7.8 ± 3.2	704	8 ± 3.4	3190	8.1 ± 3.6	1436	7.8 ± 3.5	29,693	8.4 ± 3.4	35,583	8.3 ± 3.4
Vitamin K (NDS value) (mg)	143	86 ± 46	704	102 ± 54	3190	94 ± 49	1436	71 ± 37	29,693	82 ± 38	35,583	83 ± 39
Vitamin C (mg)	143	77 ± 45	704	80 ± 49	3190	83 ± 50	1436	77 ± 49	29,693	88 ± 47	35,583	87 ± 48
Thiamin (mg)	143	1.3 ± 0.3	704	1.3 ± 0.3	3190	1.2 ± 0.3	1436	1.3 ± 0.3	29,693	1.3 ± 0.3	35,583	1.3 ± 0.3
Riboflavin (mg)	143	1.6 ± 0.4	704	1.3 ± 0.3	3190	1.5 ± 0.4	1436	1.6 ± 0.5	29,693	1.7 ± 0.4	35,583	1.6 ± 0.4
Niacin (mg)	143	16 ± 7	704	16 ± 7	3190	16 ± 7	1436	16 ± 7	29,693	17 ± 7	35,583	17 ± 7
Vitamin B_6 (mg)	143	1.5 ± 0.4	704	1.4 ± 0.4	3190	1.4 ± 0.4	1436	1.5 ± 0.4	29,693	1.6 ± 0.4	35,583	1.6 ± 0.4
Folacin (mcg)	143	213 ± 88	704	196 ± 87	3190	200 ± 95	1436	193 ± 91	29,693	228 ± 91	35,583	223 ± 92
Vitamin B_{12} (mcg)	143	4.9 ± 2.6	704	4.9 ± 2.7	3190	5.8 ± 3.4	1436	4.7 ± 2.5	29,693	5.1 ± 2.2	35,583	5.1 ± 2.4
Calcium (mg)	143	635 ± 339	704	482 ± 265	3190	515 ± 300	1436	650 ± 377	29,693	707 ± 356	35,583	678 ± 357
Total calcium (mg)	143	817 ± 492	704	772 ± 498	3190	635 ± 411	1436	823 ± 524	29,693	970 ± 550	35,583	920 ± 547
Magnesium (mg)	143	232 ± 95	704	217 ± 89	3190	211 ± 95	1436	227 ± 99	29,693	251 ± 92	35,583	245 ± 94
Iron (mg)	143	12 ± 5	704	11 ± 5	3190	11 ± 5	1436	12 ± 5	29,693	13 ± 5	35,583	12 ± 5
Zinc (mg)	143	9 ± 4	704	9 ± 4	3190	9 ± 4	1436	9 ± 4	29,693	10 ± 4	35,583	10 ± 4
Sodium (mg)	143	2541 ± 1108	704	2466 ± 1096	3190	2489 ± 1190	1436	2518 ± 1243	29,693	2672 ± 1049	35,583	2642 ± 1079
Potassium (mg)	143	2283 ± 931	704	2094 ± 889	3190	2034 ± 909	1436	2199 ± 969	29,693	2506 ± 898	35,583	2434 ± 923
Phosphorous (mg)	143	988 ± 464	704	886 ± 405	3190	904 ± 441	1436	1024 ± 497	29,693	1086 ± 445	35,583	1059 ± 452
Copper (mg)	143	1 ± 0.2	704	1 ± 0.2	3190	1 ± 0.2	1436	1 ± 0.2	29,693	1.1 ± 0.2	35,583	1.1 ± 0.2
Total carotenoids (mcg)	143	11,692 ± 6859	704	11,717 ± 6262	3190	10,358 ± 6020	1436	10,519 ± 6498	29,693	12,443 ± 6245	35,583	12,130 ± 6305
Alpha-carotene (mcg)	143	568 ± 496	704	821 ± 595	3190	503 ± 446	1436	506 ± 460	29,693	737 ± 553	35,583	702 ± 549
Beta-carotene (mcg)	143	2660 ± 1860	704	3471 ± 2205	3190	2948 ± 1986	1436	2287 ± 1664	29,693	3014 ± 1803	35,583	2981 ± 1835
Lycopene (mcg)	143	6287 ± 4360	704	5059 ± 3451	3190	4543 ± 3612	1436	5797 ± 4333	29,693	6649 ± 4062	35,583	6347 ± 4114
Lutein + zeaxanthin (mcg)	143	1392 ± 836	704	1488 ± 841	3190	1494 ± 879	1436	1184 ± 666	29,693	1328 ± 665	35,583	1338 ± 691
Fruits and vegetables (servings/day)	143	3.1 ± 1.4	704	3.1 ± 1.3	3190	3 ± 1.3	1436	2.6 ± 1.2	29,693	3.5 ± 1.4	35,583	3.4 ± 1.4
Fruits and vegetables (servings/day/1000 kcal)	143	2 ± 0.8	704	2.1 ± 0.8	3190	2 ± 0.8	1436	1.7 ± 0.7	29,693	2.2 ± 0.8	35,583	2.1 ± 0.8
Grains (servings/day)	143	4 ± 1.8	704	4.3 ± 1.7	3189	3.8 ± 1.8	1436	4.8 ± 2.4	29,692	4.2 ± 1.7	35,581	4.2 ± 1.8
Grains (servings/day/1000 kcal)	143	2.5 ± 0.7	704	2.9 ± 0.7	3189	2.4 ± 0.7	1436	2.9 ± 0.9	29,692	2.6 ± 0.6	35,581	2.6 ± 0.6

[a]Total includes those of unknown ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 15. Baseline dietary intake of WHI Observational Study participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 382)		Asian/Pacific Islander (*N* = 2497)		Black (*N* = 6749)		Hispanic (*N* = 3254)		White (*N* = 75,804)		Total[a] (*N* = 89,916)	
Nutrient[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Energy (kcal)	382	1448 ± 613	2497	1326 ± 510	6749	1383 ± 597	3254	1416 ± 620	75,804	1475 ± 525	89,916	1460 ± 537
Total fat (gm)	382	52 ± 29	2497	43 ± 22	6749	49 ± 28	3254	49 ± 28	75,804	49 ± 24	89,916	49 ± 25
Energy from fat (%)	382	32 ± 9	2497	29 ± 8	6749	32 ± 9	3254	31 ± 9	75,804	30 ± 8	89,916	30 ± 8
Total carbohydrate (gm)	382	178 ± 76	2497	178 ± 67	6749	176 ± 76	3254	179 ± 82	75,804	186 ± 69	89,916	184 ± 70
Energy from carbohydrates (%)	382	49 ± 10	2497	54 ± 9	6749	51 ± 10	3254	50 ± 11	75,804	50 ± 10	89,916	50 ± 10
Protein (gm)	382	60 ± 28	2497	54 ± 24	6749	54 ± 26	3254	58 ± 28	75,804	62 ± 24	89,916	61 ± 25
Energy from protein (%)	382	16 ± 3	2497	16 ± 3	6749	16 ± 4	3254	16 ± 3	75,804	17 ± 3	89,916	17 ± 3
Alcohol (gm)	382	1 ± 1	2497	0.4 ± 0.3	6749	0.7 ± 0.6	3254	0.9 ± 0.9	75,804	2.2 ± 2.6	89,916	1.9 ± 2.3
Energy from alcohol (%)	382	0.6 ± 0.5	2497	0.3 ± 0.2	6749	0.5 ± 0.3	3254	0.6 ± 0.4	75,804	1.3 ± 1.2	89,916	1.1 ± 1
Total PFA (gm)	382	11 ± 6	2497	10 ± 5	6749	11 ± 6	3254	10 ± 6	75,804	10 ± 5	89,916	10 ± 5
Total MFA (gm)	382	20 ± 10	2497	16 ± 8	6749	19 ± 10	3254	18 ± 10	75,804	18 ± 9	89,916	18 ± 9
Total SFA (gm)	382	18 ± 10	2497	13 ± 7	6749	16 ± 9	3254	16 ± 9	75,804	17 ± 9	89,916	16 ± 9
Energy from SFA (%)	382	11 ± 3	2497	9 ± 3	6749	10 ± 3	3254	10 ± 3	75,804	10 ± 3	89,916	10 ± 3
Total trans fatty Acid (gm)	382	3.1 ± 1.4	2497	2.2 ± 1	6749	3.3 ± 1.7	3254	2.7 ± 1.3	75,804	2.9 ± 1.3	89,916	2.9 ± 1.4
Animal protein (gm)	382	41 ± 21	2497	32 ± 18	6749	36 ± 21	3254	38 ± 22	75,804	42 ± 20	89,916	41 ± 20
Vegetable protein (gm)	382	17 ± 8	2497	20 ± 8	6749	16 ± 7	3254	18 ± 8	75,804	18 ± 7	89,916	18 ± 7
Dietary fiber (gm)	382	14 ± 6	2497	14 ± 6	6749	13 ± 6	3254	15 ± 7	75,804	16 ± 6	89,916	16 ± 6
Water soluble fiber (gm)	382	5 ± 1.8	2497	5.2 ± 1.9	6749	4.7 ± 1.8	3254	4.9 ± 1.9	75,804	5.6 ± 1.9	89,916	5.5 ± 1.9
Insoluble dietary fiber (gm)	382	9 ± 4	2497	9 ± 4	6749	9 ± 4	3254	10 ± 4	75,804	11 ± 4	89,916	10 ± 4
Cholesterol (mg)	382	191 ± 121	2497	156 ± 93	6749	174 ± 115	3254	178 ± 112	75,804	168 ± 95	89,916	168 ± 98
Total vitamin A (mcg Re)	382	7257 ± 4337	2497	8722 ± 5239	6749	7598 ± 4691	3254	6308 ± 3971	75,804	8389 ± 4448	89,916	8239 ± 4510
Vitamin D (mcg)	382	3.9 ± 2	2497	3.3 ± 1.7	6749	3.6 ± 1.8	3254	3.5 ± 1.8	75,804	4.4 ± 2.1	89,916	4.3 ± 2.1
Total alpha-toc eq (mg)	382	7 ± 3	2497	7.1 ± 2.8	6749	7 ± 3.1	3254	6.8 ± 3	75,804	7.5 ± 3	89,916	7.5 ± 3
Vitamin K (NDS value) (mg)	382	75 ± 41	2497	103 ± 59	6749	90 ± 51	3254	67 ± 37	75,804	80 ± 39	89,916	80 ± 41
Vitamin C (mg)	382	87 ± 51	2497	95 ± 56	6749	91 ± 57	3254	86 ± 54	75,804	100 ± 54	89,916	99 ± 54
Thiamin (mg)	382	1.2 ± 0.3	2497	1.2 ± 0.3	6749	1.2 ± 0.3	3254	1.2 ± 0.3	75,804	1.3 ± 0.3	89,916	1.3 ± 0.3
Riboflavin (mg)	382	1.5 ± 0.4	2497	1.2 ± 0.3	6749	1.4 ± 0.4	3254	1.5 ± 0.4	75,804	1.6 ± 0.4	89,916	1.6 ± 0.4
Niacin (mg)	382	15 ± 6	2497	15 ± 6	6749	15 ± 6	3254	15 ± 7	75,804	17 ± 6	89,916	16 ± 6
Vitamin B_6 (mg)	382	1.5 ± 0.4	2497	1.4 ± 0.3	6749	1.4 ± 0.4	3254	1.5 ± 0.4	75,804	1.6 ± 0.4	89,916	1.6 ± 0.4
Folacin (mcg)	382	210 ± 91	2497	207 ± 90	6749	203 ± 97	3254	196 ± 94	75,804	240 ± 97	89,916	234 ± 98
Vitamin B_{12} (mcg)	382	4.5 ± 2.4	2497	4.1 ± 2.2	6749	4.8 ± 2.9	3254	4.2 ± 2.2	75,804	4.6 ± 2	89,916	4.6 ± 2.1
Calcium (mg)	382	626 ± 384	2497	475 ± 267	6749	497 ± 290	3254	619 ± 369	75,804	705 ± 366	89,916	675 ± 366
Total calcium (mg)	382	857 ± 568	2497	835 ± 571	6749	633 ± 419	3254	842 ± 560	75,804	1056 ± 618	89,916	999 ± 614
Magnesium (mg)	382	225 ± 95	2497	220 ± 86	6749	207 ± 91	3254	221 ± 98	75,804	254 ± 92	89,916	247 ± 94
Iron (mg)	382	11 ± 5	2497	11 ± 5	6749	11 ± 5	3254	11 ± 5	75,804	13 ± 5	89,916	12 ± 5
Zinc (mg)	382	9 ± 4	2497	8 ± 3	6749	8 ± 4	3254	9 ± 4	75,804	10 ± 4	89,916	10 ± 4
Sodium (mg)	382	2401 ± 1157	2497	2270 ± 964	6749	2213 ± 1044	3254	2257 ± 1112	75,804	2460 ± 957	89,916	2425 ± 979
Potassium (mg)	382	2268 ± 938	2497	2113 ± 876	6749	2031 ± 898	3254	2179 ± 978	75,804	2558 ± 919	89,916	2483 ± 941
Phosphorous (mg)	382	961 ± 471	2497	835 ± 373	6749	837 ± 405	3254	951 ± 468	75,804	1045 ± 430	89,916	1016 ± 435
Copper (mg)	382	1 ± 0.2	2497	1 ± 0.2	6749	1 ± 0.2	3254	1 ± 0.2	75,804	1.1 ± 0.2	89,916	1 ± 0.2
Total carotenoids (mcg)	382	11,993 ± 7103	2497	12,376 ± 6959	6749	10,481 ± 6340	3254	10,824 ± 6764	75,804	13,129 ± 6858	89,916	12,782 ± 6898
Alpha-carotene (mcg)	382	627 ± 567	2497	896 ± 697	6749	524 ± 496	3254	547 ± 503	75,804	827 ± 647	89,916	786 ± 641
Beta-carotene (mcg)	382	2863 ± 2001	2497	3993 ± 2662	6749	3139 ± 2194	3254	2494 ± 1848	75,804	3421 ± 2147	89,916	3371 ± 2169
Lycopene (mcg)	382	6278 ± 4536	2497	4738 ± 3531	6749	4244 ± 3476	3254	5685 ± 4369	75,804	6554 ± 4315	89,916	6243 ± 4319
Lutein + zeaxanthin (mcg)	382	1326 ± 754	2497	1702 ± 1054	6749	1574 ± 994	3254	1260 ± 750	75,804	1451 ± 781	89,916	1458 ± 806
Fruits and vegetables (servings/day)	382	3.2 ± 1.4	2497	3.7 ± 1.6	6749	3.4 ± 1.6	3254	3.1 ± 1.5	75,804	4 ± 1.7	89,916	3.9 ± 1.7
Fruits and vegetables (servings/day/1000 kcal)	382	2.3 ± 1	2497	2.8 ± 1.1	6749	2.5 ± 1.1	3254	2.2 ± 1	75,804	2.8 ± 1	89,916	2.7 ± 1.1
Grains (servings/day)	382	4.1 ± 2	2497	4.3 ± 1.7	6745	3.6 ± 1.7	3253	4.4 ± 2.2	75,795	4 ± 1.7	89,901	4 ± 1.7
Grains (servings/day/1000 kcal)	382	2.8 ± 0.8	2497	3.2 ± 0.8	6745	2.5 ± 0.8	3253	3.1 ± 0.9	75,795	2.7 ± 0.7	89,901	2.7 ± 0.8

[a]Total includes those of unknown ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 16. Baseline blood analytes from a random sample of WHI Estrogen + Progestin participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 25)		Asian/Pacific Islander (*N* = 113)		Black (*N* = 255)		Hispanic (*N* = 185)		White (*N* = 714)		Total[a] (*N* = 1319)	
Blood Analyte[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Total cholesterol (mg/dl)	25	208.3 ± 40	113	220.5 ± 33	255	217.6 ± 41.5	185	223.3 ± 37.9	713	222.7 ± 36.3	1318	222 ± 37.1
LDL-C (mg/dl)	25	122.5 ± 39.1	112	129.2 ± 30.1	253	134.6 ± 41.1	181	135 ± 37	699	135 ± 32.1	1297	134.7 ± 32.9
HDL-C (mg/dl)	25	51.5 ± 13.8	113	57.9 ± 14.9	254	55.2 ± 12.7	185	51.9 ± 12.1	709	55.5 ± 13.9	1313	55.3 ± 13.6
HDL-2 (mg/dl)	25	15.4 ± 5.8	112	17.3 ± 7.7	248	15.9 ± 6.7	182	14.3 ± 6.8	683	16.6 ± 7.2	1276	16.4 ± 7
HDL-3 (mg/dl)	25	35.9 ± 8.7	112	39.8 ± 8.1	248	38.7 ± 7.1	182	36.7 ± 7.1	683	38.2 ± 8.1	1276	38.2 ± 7.9
Triglyceride (mg/dl)	25	133.1 ± 68.2	113	133.4 ± 61.2	255	108.6 ± 47.6	185	150.3 ± 66.9	713	132.5 ± 61	1318	130.9 ± 59.4
LP(a) (mg/dl)	25	8.1 ± 10	112	13.1 ± 13.1	249	28.4 ± 25.8	185	11.9 ± 14.2	701	15.4 ± 16.9	1299	16 ± 17.2
Retinol (μg/ml)	25	0.5 ± 0.12	113	0.59 ± 0.14	255	0.54 ± 0.15	185	0.55 ± 0.14	714	0.59 ± 0.14	1318	0.59 ± 0.14
Alpha-carotene (μg/ml)	25	0.04 ± 0.03	113	0.1 ± 0.06	255	0.04 ± 0.04	185	0.07 ± 0.06	714	0.07 ± 0.05	1318	0.06 ± 0.05
Beta-carotene (μg/ml)	25	0.19 ± 0.16	113	0.44 ± 0.29	255	0.23 ± 0.19	185	0.24 ± 0.18	714	0.26 ± 0.2	1318	0.26 ± 0.2
Beta-cryptoxanthine (μg/ml)	25	0.05 ± 0.03	113	0.17 ± 0.14	255	0.07 ± 0.05	185	0.1 ± 0.07	714	0.07 ± 0.05	1318	0.07 ± 0.05
Lycopene (μg/ml)	25	0.35 ± 0.15	113	0.34 ± 0.23	255	0.34 ± 0.21	185	0.4 ± 0.22	714	0.36 ± 0.2	1318	0.36 ± 0.19
Lutein and zeaxanthin (μg/ml)	25	0.16 ± 0.08	113	0.26 ± 0.11	255	0.2 ± 0.1	185	0.2 ± 0.09	714	0.19 ± 0.08	1318	0.19 ± 0.08
Alpha-tocopherol (μg/ml)	25	12.1 ± 4.2	113	17.1 ± 7.3	255	13.4 ± 5.3	185	14.7 ± 5.3	714	15.1 ± 6.2	1318	15 ± 6
Gamma-tocopherol (μg/ml)	25	2.7 ± 1.3	113	1.1 ± 1	255	2 ± 1.4	185	1.8 ± 1.2	714	1.7 ± 1.4	1318	1.7 ± 1.3
Factor VII activity, antigen (%)	22	118 ± 31.5	111	120.6 ± 26.2	243	110.4 ± 28.6	174	120.4 ± 30	694	121.9 ± 28.3	1271	120.7 ± 28.4
Factor VIIC (%)	22	116.2 ± 30.4	111	122.7 ± 24.3	237	113.5 ± 29.1	167	120.3 ± 28	688	123.4 ± 25.9	1252	122.2 ± 26.3
Fibrinogen (mg/dl)	22	313.1 ± 69.6	111	295.3 ± 56.4	243	312.8 ± 66.1	174	313.2 ± 64.7	692	299.7 ± 54.4	1269	301.5 ± 56.2
Glucose (mg/dl)	25	107.1 ± 31.6	113	100.1 ± 18.8	255	104.2 ± 28.2	185	102.4 ± 23.7	710	97.5 ± 17.6	1315	98.4 ± 19
Insulin (μIU/ml)	25	10.5 ± 6.1	108	8.9 ± 4.8	252	11.7 ± 5.8	184	11.9 ± 6	684	9.8 ± 4.8	1280	10 ± 4.9

HDL, high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein.
[a]Total includes those of unknown ethnicity. Means and standard deviations are weighted by ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 17. Baseline blood analytes from a random sample of WHI Estrogen-Alone participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 27)		Asian/Pacific Islander (*N* = 44)		Black (*N* = 332)		Hispanic (*N* = 143)		White (*N* = 423)		Total[a] (*N* = 992)	
Blood Analyte[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Total cholesterol (mg/dl)	26	233.8 ± 40.2	44	232.8 ± 32.6	332	221.6 ± 41.4	143	215.3 ± 39.1	423	227.2 ± 40.3	991	226.5 ± 41.3
LDL-C (mg/dl)	24	141.2 ± 30.6	42	135.6 ± 34.2	331	139.2 ± 39.7	141	127.5 ± 33.7	410	137.4 ± 37.9	970	137.3 ± 37.8
HDL-C (mg/dl)	26	53.5 ± 12.8	44	57.8 ± 16	331	55.6 ± 12.8	142	52.9 ± 12.5	421	54 ± 14	987	54.2 ± 13.8
HDL-2 (mg/dl)	26	16.1 ± 5.5	43	16.4 ± 8.4	329	16.6 ± 6.6	142	15.2 ± 6.4	400	15.8 ± 6.8	963	15.9 ± 6.7
HDL-3 (mg/dl)	27	37 ± 7.6	43	40.2 ± 8.7	329	38.4 ± 7.9	142	37.1 ± 7.6	400	37.7 ± 8.4	964	37.8 ± 8.3
Triglyceride (mg/dl)	26	155 ± 79	44	158.8 ± 77.8	332	108.6 ± 43.7	143	147.3 ± 59.5	423	148 ± 70.4	991	144.1 ± 67.3
LP(a) (mg/dl)	26	16.4 ± 21.5	44	17 ± 12.1	326	28 ± 26.4	141	10.3 ± 11.1	414	15.5 ± 16.8	974	16.1 ± 17.2
Retinol (μg/ml)	27	0.58 ± 0.17	44	0.6 ± 0.13	332	0.54 ± 0.14	143	0.5 ± 0.14	423	0.6 ± 0.14	992	0.59 ± 0.14
Alpha-carotene (μg/ml)	27	0.05 ± 0.04	44	0.09 ± 0.08	332	0.05 ± 0.04	143	0.07 ± 0.06	423	0.05 ± 0.04	992	0.05 ± 0.04
Beta-carotene (μg/ml)	27	0.22 ± 0.21	44	0.4 ± 0.3	331	0.26 ± 0.2	143	0.21 ± 0.2	423	0.21 ± 0.15	991	0.22 ± 0.16
Beta-cryptoxanthine (μg/ml)	27	0.07 ± 0.05	44	0.12 ± 0.09	332	0.07 ± 0.04	143	0.09 ± 0.08	423	0.06 ± 0.04	992	0.06 ± 0.04
Lycopene (μg/ml)	27	0.32 ± 0.16	44	0.36 ± 0.21	332	0.32 ± 0.22	143	0.35 ± 0.19	423	0.35 ± 0.19	992	0.35 ± 0.19
Lutein and zeaxanthin (μg/ml)	27	0.19 ± 0.1	44	0.27 ± 0.13	332	0.22 ± 0.1	143	0.18 ± 0.08	423	0.18 ± 0.08	992	0.18 ± 0.08
Alpha-tocopherol (μg/ml)	27	16.2 ± 7.3	44	18.9 ± 7.9	332	13.3 ± 5	143	14.1 ± 6.1	423	15 ± 6.2	992	14.9 ± 6
Gamma-tocopherol (μg/ml)	27	2 ± 1.7	44	1.2 ± 0.9	332	2.1 ± 1.4	143	1.8 ± 1.3	423	2 ± 1.5	992	1.9 ± 1.5
Factor VII activity, antigen (%)	25	135.3 ± 32.4	42	125.7 ± 23.7	324	111 ± 23.4	136	118.8 ± 25.7	412	128.6 ± 28.4	962	126.5 ± 28.4
Factor VIIC (%)	25	133 ± 26.6	42	125.6 ± 23.1	314	114.8 ± 26	131	121 ± 27.4	409	128.9 ± 26.5	943	127.1 ± 27
Fibrinogen (mg/dl)	25	326.9 ± 57.3	42	290.2 ± 55.6	324	319.9 ± 62.7	136	310.3 ± 71.5	410	303.9 ± 60.3	960	305.6 ± 62
Glucose (mg/dl)	27	110 ± 33.5	44	103.4 ± 21.7	331	105.8 ± 29.4	141	100.3 ± 23.2	423	101.5 ± 23.3	989	101.9 ± 23.9
Insulin (μIU/ml)	27	12 ± 6.8	43	10.3 ± 6.1	324	12.6 ± 6.6	140	11.8 ± 6.2	414	10.8 ± 5.5	971	11 ± 5.5

HDL, high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein.
[a]Total includes those of unknown ethnicity. Means and standard deviations are weighted by ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 18. Baseline blood analytes from a random sample of WHI Dietary Modification participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 58)		Asian/Pacific Islander (*N* = 173)		Black (*N* = 622)		Hispanic (*N* = 260)		White (*N* = 1201)		Total[a] (*N* = 2398)	
Blood Analyte[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Total cholesterol (mg/dl)	57	216.7 ± 37.1	172	217.9 ± 35.8	662	216.3 ± 40.8	260	213.4 ± 36.2	1201	222.2 ± 36.9	2395	221.2 ± 37.1
LDL-C (mg/dl)	56	124.2 ± 35.7	166	123.5 ± 35.7	662	132.1 ± 39.4	256	125.3 ± 34.8	1171	128.9 ± 35.2	2352	128.8 ± 35
HDL-C (mg/dl)	57	54 ± 15.9	172	56.7 ± 13.4	662	57.1 ± 14	260	52.9 ± 12	1195	58 ± 15.4	2389	57.6 ± 14.9
HDL-2 (mg/dl)	55	16.3 ± 7.4	168	16.9 ± 7.3	653	17.2 ± 7.2	257	14.9 ± 6.3	1159	17.2 ± 7.7	2335	17 ± 7.4
HDL-3 (mg/dl)	56	38 ± 8.2	168	39.4 ± 7.9	653	39.3 ± 8.2	257	37.2 ± 7.5	1160	40.3 ± 9.2	2337	40 ± 8.9
Triglyceride (mg/dl)	57	155.9 ± 68.3	172	153.9 ± 72.3	662	108 ± 43.2	260	148.4 ± 62.6	1201	142.2 ± 66.7	2395	139.3 ± 64
LP(a) (mg/dl)	56	10.5 ± 13.4	169	13.2 ± 11.1	652	27.9 ± 24.3	260	11 ± 13.1	1183	14.3 ± 16.1	2364	15 ± 16.5
Retinol (μg/ml)	58	0.59 ± 0.15	173	0.59 ± 0.14	662	0.53 ± 0.14	260	0.53 ± 0.14	1199	0.61 ± 0.14	2396	0.6 ± 0.14
Alpha-carotene (μg/ml)	58	0.04 ± 0.04	173	0.08 ± 0.06	662	0.04 ± 0.04	260	0.07 ± 0.05	1199	0.06 ± 0.05	2396	0.06 ± 0.05
Beta-carotene (μg/ml)	58	0.2 ± 0.16	173	0.32 ± 0.24	662	0.24 ± 0.17	260	0.21 ± 0.17	1199	0.22 ± 0.17	2396	0.22 ± 0.17
Beta-cryptoxanthine (μg/ml)	58	0.06 ± 0.03	173	0.13 ± 0.1	662	0.07 ± 0.05	260	0.08 ± 0.06	1199	0.07 ± 0.04	2396	0.07 ± 0.05
Lycopene (μg/ml)	58	0.32 ± 0.16	173	0.33 ± 0.19	662	0.34 ± 0.21	260	0.37 ± 0.2	1199	0.38 ± 0.18	2396	0.37 ± 0.18
Lutein and zeaxanthin (μg/ml)	58	0.18 ± 0.08	173	0.25 ± 0.1	662	0.22 ± 0.1	260	0.18 ± 0.08	1199	0.19 ± 0.09	2396	0.19 ± 0.09
Alpha-tocopherol (μg/ml)	58	15.7 ± 6.5	173	17.4 ± 7.4	662	13 ± 4.8	260	14.6 ± 5.8	1199	15.2 ± 5.7	2396	15 ± 5.5
Gamma-tocopherol (μg/ml)	58	1.8 ± 1.3	173	1.3 ± 1	662	2.1 ± 1.4	260	1.7 ± 1.2	1199	1.7 ± 1.3	2396	1.7 ± 1.3
Factor VII activity, antigen (%)	56	132.9 ± 33.3	168	128.4 ± 28.6	641	111.3 ± 27.7	252	118.9 ± 28.5	1162	129.2 ± 32.9	2323	127 ± 32.2
Factor VIIC (%)	56	125.2 ± 29.1	168	124.2 ± 24.6	623	114.3 ± 28.9	245	117.8 ± 28.5	1144	127.8 ± 31.8	2280	125.9 ± 31.1
Fibrinogen (mg/dl)	56	300.4 ± 64.4	169	286.9 ± 56.2	641	316 ± 65.8	252	301.4 ± 62.9	1155	291.4 ± 56.4	2317	294 ± 57.4
Glucose (mg/dl)	58	102.7 ± 20.4	173	99.2 ± 15.5	662	102.2 ± 25.9	259	99.3 ± 23.4	1200	97.2 ± 18.1	2396	97.9 ± 19
Insulin (μIU/ml)	55	11.5 ± 5.9	169	9.1 ± 4.4	654	12.1 ± 6.1	254	11.7 ± 6.3	1168	9.7 ± 4.9	2344	10 ± 5

HDL, high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein.
[a]Total includes those of unknown ethnicity. Means and standard deviations are weighted by ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 19. Baseline blood analytes from a random sample of WHI Calcium and Vitamin D participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 53)		Asian/Pacific Islander (*N* = 161)		Black (*N* = 538)		Hispanic (*N* = 287)		White (*N* = 1125)		Total[a] (*N* = 2202)	
Blood Analyte[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Total cholesterol (mg/dl)	52	215.6 ± 36.2	161	223.5 ± 35.6	538	215.6 ± 41.6	287	218 ± 36.4	1125	223.4 ± 36.1	2201	222.3 ± 36.6
LDL-C (mg/dl)	52	124.6 ± 35.5	156	130 ± 36.2	536	131.6 ± 41.1	283	128.9 ± 34.5	1099	131.7 ± 35	2163	131.4 ± 35
HDL-C (mg/dl)	52	52.7 ± 16.4	161	57 ± 13.8	537	56.7 ± 14.3	286	53.3 ± 12.4	1121	56.9 ± 15.1	2195	56.7 ± 14.7
HDL-2 (mg/dl)	50	16.4 ± 6.6	158	17 ± 7.4	528	16.7 ± 7.3	282	14.7 ± 6.9	1080	16.9 ± 7.7	2135	16.8 ± 7.5
HDL-3 (mg/dl)	51	36.9 ± 9.3	158	39.4 ± 7.9	528	39.4 ± 8.3	282	37.7 ± 7.4	1081	39.5 ± 8.9	2137	39.3 ± 8.6
Triglyceride (mg/dl)	52	153.6 ± 70.4	161	149 ± 67.1	538	106.9 ± 44.6	287	149.9 ± 61.4	1125	139.7 ± 66	2201	137 ± 63.4
LP(a) (mg/dl)	51	8.5 ± 11.1	159	14.1 ± 12	528	26.6 ± 24.5	286	10.8 ± 12.3	1109	14.3 ± 16.1	2171	14.9 ± 16.4
Retinol (μg/ml)	53	0.57 ± 0.14	161	0.6 ± 0.14	538	0.53 ± 0.14	287	0.53 ± 0.14	1125	0.6 ± 0.14	2201	0.59 ± 0.14
Alpha-carotene (μg/ml)	53	0.04 ± 0.03	161	0.09 ± 0.06	538	0.04 ± 0.04	287	0.07 ± 0.05	1125	0.06 ± 0.05	2201	0.06 ± 0.05
Beta-carotene (μg/ml)	53	0.21 ± 0.19	161	0.38 ± 0.28	538	0.23 ± 0.18	287	0.21 ± 0.18	1125	0.23 ± 0.17	2201	0.23 ± 0.17
Beta-cryptoxanthine (μg/ml)	53	0.05 ± 0.03	161	0.14 ± 0.11	538	0.07 ± 0.04	287	0.09 ± 0.07	1125	0.07 ± 0.05	2201	0.07 ± 0.05
Lycopene (μg/ml)	53	0.34 ± 0.15	161	0.35 ± 0.22	538	0.32 ± 0.22	287	0.37 ± 0.21	1125	0.37 ± 0.19	2201	0.37 ± 0.19
Lutein and Zeaxanthin (μg/ml)	53	0.18 ± 0.09	161	0.26 ± 0.11	538	0.21 ± 0.1	287	0.19 ± 0.09	1125	0.19 ± 0.08	2201	0.19 ± 0.08
Alpha-tocopherol (μg/ml)	53	15.9 ± 6.8	161	18 ± 8	538	13.2 ± 5.2	287	14.7 ± 5.6	1125	15.2 ± 5.9	2201	15 ± 5.7
Gamma-tocopherol (μg/ml)	53	1.9 ± 1.3	161	1.2 ± 1	538	2 ± 1.4	287	1.8 ± 1.2	1125	1.8 ± 1.3	2201	1.8 ± 1.3
Factor VII activity, antigen (%)	48	130.1 ± 32.9	158	124.6 ± 26.6	522	110.1 ± 27.1	272	120.4 ± 29.6	1093	128.4 ± 32	2131	126.1 ± 31.4
Factor VIIC (%)	48	123.8 ± 31.4	158	123.5 ± 24.4	502	114.3 ± 29.1	263	119.1 ± 27.8	1081	126.7 ± 30	2089	125.1 ± 29.6
Fibrinogen (mg/dl)	48	303.3 ± 65.5	159	287.5 ± 55.1	522	319.2 ± 64.3	272	304 ± 65.6	1092	294.9 ± 56.4	2131	297.3 ± 57.4
Glucose (mg/dl)	53	104.5 ± 26.4	161	100.5 ± 18.1	537	100.9 ± 25.3	285	99.4 ± 23.4	1124	98.2 ± 19.4	2198	98.6 ± 20
Insulin (μIU/ml)	51	10.7 ± 6	158	9.3 ± 4.9	532	12.2 ± 6.5	283	11.2 ± 5.8	1093	9.9 ± 4.9	2155	10.1 ± 5

HDL, high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein.
[a]Total includes those of unknown ethnicity. Means and standard deviations are weighted by ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

APPENDIX TABLE 20. Baseline blood analytes from a random sample of WHI Observational Study participants by race/ethnicity

	Race/Ethnicity											
	American Indian (*N* = 13)		Asian/Pacific Islander (*N* = 74)		Black (*N* = 133)		Hispanic (*N* = 145)		White (*N* = 697)		Total[a] (*N* = 1062)	
Blood Analyte[b]	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD	*N*	Mean ± SD
Total cholesterol (mg/dl)	13	218.3 ± 45.4	74	209.1 ± 36.6	133	215.3 ± 37.2	145	214.8 ± 38.4	697	215.7 ± 35.4	1062	215.4 ± 36.7
LDL-C (mg/dl)	12	123.7 ± 52.9	73	112.6 ± 34.2	131	127.4 ± 37.1	142	121.3 ± 35.3	684	119.9 ± 33.6	1042	120.4 ± 33.8
HDL-C (mg/dl)	13	54.5 ± 12.4	74	62.6 ± 14.6	133	60.3 ± 16.3	145	56.6 ± 15.2	696	61.8 ± 16.7	1061	61.4 ± 16.5
HDL-2 (mg/dl)	13	15.4 ± 8.5	72	20.4 ± 7.2	133	19.2 ± 8.5	141	17.5 ± 7.9	674	19.9 ± 9.3	1033	19.7 ± 9
HDL-3 (mg/dl)	13	37.7 ± 7.7	72	41.6 ± 9.2	133	40.3 ± 9.2	141	38.4 ± 8.8	674	41 ± 9	1033	40.8 ± 9
Triglyceride (mg/dl)	13	136 ± 58.2	74	141.5 ± 63.2	133	107.7 ± 47.3	145	149.1 ± 70.1	697	133.8 ± 62.2	1062	132.1 ± 60.8
LP(a) (mg/dl)	13	22.4 ± 21	74	14.2 ± 13.5	133	33.4 ± 30.4	145	18.3 ± 18.2	694	15.4 ± 17	1059	16.6 ± 17.9
Retinol (μg/ml)	13	0.6 ± 0.2	74	0.59 ± 0.14	133	0.54 ± 0.14	145	0.59 ± 0.15	696	0.62 ± 0.14	1061	0.61 ± 0.14
Alpha-carotene (μg/ml)	13	0.06 ± 0.04	74	0.12 ± 0.07	133	0.05 ± 0.04	145	0.08 ± 0.06	696	0.08 ± 0.06	1061	0.08 ± 0.06
Beta-carotene (μg/ml)	13	0.23 ± 0.14	74	0.41 ± 0.35	133	0.27 ± 0.19	145	0.23 ± 0.2	696	0.25 ± 0.22	1061	0.26 ± 0.21
Beta-cryptoxanthine (μg/ml)	13	0.07 ± 0.05	74	0.17 ± 0.15	133	0.08 ± 0.05	145	0.09 ± 0.07	696	0.08 ± 0.05	1061	0.08 ± 0.05
Lycopene (μg/ml)	13	0.41 ± 0.26	74	0.35 ± 0.18	133	0.32 ± 0.21	145	0.36 ± 0.18	696	0.37 ± 0.21	1061	0.36 ± 0.21
Lutein and zeaxanthin (μg/ml)	13	0.2 ± 0.06	74	0.25 ± 0.1	133	0.22 ± 0.11	145	0.21 ± 0.09	696	0.2 ± 0.1	1061	0.21 ± 0.1
Alpha-tocopherol (μg/ml)	13	17.6 ± 6.9	74	17.8 ± 6.1	133	13.8 ± 4.7	145	16.8 ± 6.3	696	17.2 ± 6.9	1061	16.9 ± 6.6
Gamma-tocopherol (μg/ml)	13	1.4 ± 1.5	74	0.9 ± 0.7	133	1.7 ± 1.2	145	1.3 ± 1.1	696	1.2 ± 1	1061	1.3 ± 1
Factor VII activity, antigen (%)	13	130.4 ± 37.2	71	122.4 ± 25.8	128	110.2 ± 27.2	136	125.3 ± 29.7	681	125.2 ± 30.4	1029	123.7 ± 30.3
Factor VIIC (%)	13	123.6 ± 29.3	70	116.9 ± 25.4	125	113.9 ± 27.1	130	125 ± 28.5	663	123.7 ± 30.2	1001	122.6 ± 29.9
Fibrinogen (mg/dl)	13	304.5 ± 69.9	71	283.7 ± 57	129	304.4 ± 63.9	136	297.5 ± 68	679	290.8 ± 55.1	1028	292.1 ± 57.6
Glucose (mg/dl)	13	106.4 ± 46.2	74	95.5 ± 13.6	130	102.1 ± 25.9	144	96.8 ± 22	694	93.2 ± 15.2	1055	94.3 ± 17.1
Insulin (μIU/ml)	13	10.2 ± 4.6	73	9 ± 4.3	128	11.5 ± 6.2	139	10.3 ± 5.7	654	8.5 ± 4	1007	8.8 ± 4.3

HDL, high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein.
[a]Total includes those of unknown ethnicity. Means and standard deviations are weighted by ethnicity.
[b]Means and standard deviations were computed on the log scale and back-transformed values are reported.

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