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Comparing hormone therapy effects in two RCTs and two large observational studies that used similar methods for comprehensive data collection and outcome assessment

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ABSTRACT

Objectives: Prospective observational studies (OSs) that collect adequate information about confounders can validly assess treatment consequences. However, what constitutes adequate information is unknown. This study investigated whether the extensive information collected by the Women's Health Initiative (WHI) in two OSs and two randomised controlled trials (RCTs) was adequate.

Design: Secondary analysis of WHI data. Cox regression was used to select from all baseline risk factors those that best predicted outcome. Cox regression that included these risk factors was used for two types of analyses: (1) comparing RCT and OS assessments of the effects of hormone therapy on outcome for participants with specific characteristics and (2) evaluating whether adjustment for measured confounders could eliminate outcome differences among datasets.

Setting: The WHI included more than 800 baseline risk factors and outcomes during a median follow-up of 8 years.

Participants: 151 870 postmenopausal women ages 50–79.

Primary and secondary outcome measures: Myocardial infarction and stroke.

Results: RCT and OS results differed for the association of hormone therapy with outcome after adjusting for confounding factors and stratifying on factors that were hypothesised to modulate the effects of hormone therapy (eg, age and time since menopause) or that empirically modulated the effects of hormone therapy in this dataset (eg, blood pressure, previous coronary revascularisation and private medical insurance). Some of the four WHI datasets had significantly worse outcomes than others even after adjusting for risk and stratifying by type of hormone therapy, for example, the risk-adjusted HR for myocardial infarction was 1.37 ($p<0.0001$) in an RCT placebo group compared with an OS group not taking hormone therapy.

Conclusions: Apparently the WHI did not collect sufficient information to give reliable assessments of treatment effects. If the WHI did not collect sufficient data, it is likely that few OSs collect sufficient information.

ARTICLE SUMMARY

Article focus

- Observational studies (OSs) are frequently used to compare outcomes of patients who choose different treatments.
- Results of OSs may be invalid because of confounding due to an association between patient risk and treatment choice.
- The present study assessed whether the extensive information collected by the Women's Health Initiative (WHI) was adequate to eliminate confounding and give valid results.

Key messages

- The effects of hormone therapy on stroke and myocardial infarction differ for OSs and randomised controlled trials even after taking advantage of extensive participant information to remove confounding and to select similar participants.
- Participants who self-selected for different studies had different outcomes that could not be explained by differences in measured risk factors.
- As comprehensive data such as collected by the WHI appear to be inadequate to ensure the validity of an observational study, it is unclear what observational study results can be accepted with confidence.

Strengths and limitations of this study

- The WHI dataset is unusually comprehensive and provided a good test of whether excellent datasets can ensure valid results for an observational study. The conditions for valid OSs were not identified.

Medical practice often depends on observational studies (OSs) that compare outcomes of similar patients treated differently. However, OS results may be erroneous because patient risk factors are confounded with treatment choice. Only if confounding

factors can be adequately measured, can their effects be removed with statistical methods. The success of removing confounding errors has been vigorously debated.[1–3]

The strongest evidence against the validity of the OSs has been discrepancies between OSs and randomised controlled trials (RCTs). In particular, RCTs from the Women's Health Initiative (WHI) found that hormone therapy (HT) increased the risk of myocardial infarction (MI)[4] or had no effect[5] and increased the risk of stroke.[4 5] These findings contradicted a large body of well-performed OSs suggesting that HT may reduce the risk of cardiovascular disease by 30–50%.[6–8]

However, RCT/OS discrepancies do not prove that the OS design is invalid. Another possibility is that the discrepancies are caused by differences in characteristics of the study population, therapy or outcome measurements (eg, duration of follow-up). For example, the women evaluated in the WHI RCT were older than those in most OSs, and there is some evidence that HT has a greater adverse effect on older women or women who began HT several years after menopause.[9–12] There is also evidence that the influence of HT on MI risk is greatest soon after initiation,[13] and OSs that can follow participants soon after they begin therapy may give results similar to RCTs.[10 14] It may be possible that other patient characteristics (eg, obesity, smoking or health status) that differ between types of studies alter the associations between HT and outcomes.

The WHI offers an excellent opportunity to assess the value of OSs for three reasons: (1) The same type of data were collected in almost the same way for two RCTs and two OSs of HT; (2) the data collected included comprehensive information about numerous potentially relevant risk factors that are rarely available in OSs, including many often suspected to cause confounding (eg, those related to socioeconomic status, functional status, psychological status, lifestyle factors and healthcare behaviours) and (3) the sample sizes were large enough to enable subgroup comparisons.

METHODS

The ability of an OS to eliminate confounding was examined by testing three hypotheses:

1. Result differences between OSs and RCTs can be eliminated by adjusting for the WHI risk factors.
2. Differences between OSs and RCTs are caused by differences in modulating factors such as the time after menopause that HT is initiated,[9–12] the time OS participants are on HT prior to beginning the study[13 14] or other participant characteristics that have not been previously suggested.
3. Confounding factors associated with which specific WHI study recruited the participant can be eliminated by adjusting for the WHI risk factors.

WHI dataset

Data were obtained from the WHI, which has been described in detail.[5 6] The study was approved by institutional review boards, and all participants signed informed consent forms. In brief, it was a long-term national health study that focused on strategies for preventing heart disease, breast and colorectal cancer and osteoporosis in postmenopausal women. Women aged 50–79 were enrolled from 1993 to 1998 at 40 clinical centres throughout the USA for clinical trials. Women were asked to enrol in an RCT and those who were not ineligible or not interested were given the opportunity to enrol in the WHI OS.

There were four WHI studies relevant to the present analysis: (1) an RCT of oestrogen therapy (E-alone) for women without a uterus, (2) an RCT of oestrogen plus progesterone (E+P) for women with a uterus, (3) an RCT of diet and (4) WHI OS with no interventions. The RCT of diet served as a second OS for the effects of HT because HT use was not randomised for these patients. Participants who were enrolled in the RCT for diet as well as an RCT for HT were considered to be only in the RCT for HT dataset.

For follow-up and outcome ascertainment all participants completed a self-administered, self-report. This report was completed semiannually by the RCT participants and annually by the OS participants. Adjudicated outcomes were based on medical records, autopsy reports and death certificates.

The more than 800 baseline risk factors analysed in the present study were in the following categories: demographics, general health, clinical and anthropometric, functional status, healthcare behaviours, reproductive, medical history, family history, personal habits, thoughts and feelings, therapeutic class of medication, hormones, supplements and dietary intake.

Statistical analysis

The Cox proportional hazard regression analysis was used to test the association between outcome and the primary risk factor after adjusting for covariables. The outcomes analysed in this study were MI or stroke that developed after the participants were enrolled in the study. The primary risk factors were HT (either the binary variable for any HT use or the three category variable for use of E-alone, E+P or neither) or the categorical variable for the four datasets.

The primary risk factors were represented by an indicator variable for every category except the reference category. The HR associated with an indicator variable for a category represented the risk for participants with that variable compared with the risk of participants in the reference category. The reference category for the HT variables was no HT use, and the reference category for dataset was the WHI OS.

To identify which covariables should be included in a Cox model, we first tested the statistical significance of more than 800 risk factors by including only the risk factor and age in the Cox model for a given outcome. All risk factors that were statistically significant at the $p<0.01$ level after adjusting for age alone were then

included in a backwards stepwise Cox proportional hazard regression analysis, and variables that remained statistically significant at the p<0.0001 level were retained in the model. We then used the Cox forward stepwise procedure to test whether any of the variables not already in the model could enter at the p<0.0001 level. It is unlikely that many of these variables were significant by chance alone and even less likely that adjusting for spurious variables would distort the association between HT and outcome.

To identify which risk factors modulated the association between HT and outcome we tested the interactions of HT with the risk factors that had been tested with the timing hypothesis or that had a statistically significant association with outcome at the p<0.01 level after adjusting for age and dataset.

In an analysis that only included OS participants not taking HT at baseline, follow-up began at the time the participant completed the questionnaire that first reported HT or, if they never began HT, follow-up began at the time they completed their first questionnaire after baseline. (If follow-up for these participants had begun as late as it did for the HT participants, it would have diminished the HR associated with HT.) The baseline age of participants in this analysis was computed for the time that follow-up began.

Stepwise procedures were used to find a logistic regression equation that included the risk factors independently associated at the p<0.0001 level with taking baseline HT in the WHI OS. An individual's propensity score was the probability derived from her characteristics and the estimated parameters in this equation. We evaluated whether grouping participants with similar propensity scores decreased confounding in the OSs so that OS and RCT results became more similar.

The median follow-up time was 8 years. However, for the E+P RCT, treatment was ended after a mean follow-up of 5.2 years even though follow-up on all participants was continued. To make time on HT in the study comparable for the OS and each RCT, we ended follow-up at 5 years.

All statistical analyses were performed using SAS V.9 (SAS Institute Inc, Cary, North Carolina, USA).

Sample size

Participants available for analysis included 161 748 WHI participants: 93 651from the observational study, 16 590 from the RCT of oestrogen plus progesterone (E+P), 10 722 from the RCT of oestrogen only (oestrogen-alone) and 40 785 additional women who were in the diet study and not in an RCT of HT. Of the 161 748 WHI participants, 9584 were excluded because they did not meet the following RCT exclusion criteria: platelets less than 75 000/mm^3, haematocrit less than 32%, oral daily use of a glucocorticosteroid, body mass index less than 18, systolic blood pressure greater than 200 mm Hg, diastolic blood pressure greater than 105 mm Hg, breast cancer ever, other cancers in the last 10 years, or stroke, transient ischaemic attack (TIA) or MI in the past 6 months. An additional 294 were missing information on the use of HT at baseline.

Missing data for the covariables were imputed by the mean value for ordinal or binary variables and the mode value for variables with three or more categories. After determining which risk factors were independently associated with a given outcome at the p<0.0001 level, we created a corresponding indicator variable for each of those risk factors that indicated if the variable was missing. If the missing indicator variable was statistically significant at the p<0.05 level, participants missing the corresponding risk factor were excluded. There were 146 936 participants included in the fully adjusted Cox model for MI and 149 470 included in the fully adjusted Cox model for stroke. The ability of the Cox model to predict outcome as measured by the C statistic was not improved by excluding participants with estimated values of the covariates.

RESULTS

Baseline participant characteristics for participants in the four datasets are compared in table 1. For two datasets participants on HT were compared with participants without HT. That was not necessary, however, for the RCTs for E+P and for E-alone because randomisation in these studies made the treatment arm unrelated to baseline characteristics. In the OS and RCT for diet datasets the risks due to age, race, income, educational level, physical functioning and smoking were most favourable for participants on E+P and least favourable for participants not taking HT. With the exception of smoking these characteristics were also more favourable for participants in the RCT for E+P than in the RCT for E-alone. Both socioeconomic status variables (education and income levels) are lower for the two RCTs of HT datasets than for the other two datasets, p<0.0001. For this reason it was important to evaluate whether socioeconomic status influenced the association between HT and outcome.

Propensity score

The logistic regression equation to predict the probability that a participant in the OS used HT (ie, the propensity score) included 94 independent risk factors statistically significant at the p<0.0001 level and had a C statistic of 0.90, indicating that the equation was highly predictive of HT use.

Risk factors for MI and stroke

We identified 16 risk factors (in addition to dataset) that were independently associated with MI at the p≤0.0001 level. The variables and their associated χ^2 value for the full dataset in parenthesis were age (594.3), taking medication for diabetes (284.3), smoking at baseline (182.4), systolic blood pressure (150.1), history of coronary artery bypass surgery (110.1), history of cardiovascular disease

Table 1 Percentage of participants in a given category by dataset and type of hormone therapy

	WHI OS			RCT for diet			RCTs for HT	
Variables	**E+P**	**E-alone**	**No HT**	**E+P**	**E-alone**	**No HT**	**E+P**	**E-alone**
Sample size	17 618	21 659	44 597	8907	11 880	19 968	16 581	10 719
Age (years)								
≤55	25.6	19.0	13.4	27.1	20.6	14.7	16.6	16.4
>70	9.3	16.8	25.0	5.6	11.5	17.8	17.8	20.1
Race								
Non-white	11.3	15.5	19.8	10.8	15.5	22.4	16.0	24.7
Family income								
<$35 000	23.0	33.4	42.7	23.4	33.9	41.9	45.3	54.5
>$75 000	29.1	20.0	14.5	27.4	18.8	13.7	12.5	8.1
Education level								
≤HS grad	13.2	20.8	24.8	13.7	21.6	23.5	26.1	32.4
Col grad	54.1	38.4	38.1	50.7	35.3	37.0	34.6	23.7
P Funct >75	80.2	68.8	68.2	78.4	67.7	67.4	73.6	61.5
Med visit	84.4	85.3	76.7	85.7	86.0	76.2	68.5	72.3
Smoking								
Past	46.0	42.7	40.1	44.6	42.0	40.2	39.2	38.0
Current	5.1	5.5	7.0	5.5	5.6	6.8	10.3	10.3
Meno sympt	77.3	70.4	64.8	70.9	64.3	59.5	61.9	60.5

All characteristics differed among the four datasets and among treatment groups within the observational study and RCT for diet datasets at the p<0.0001 level.
Col, college; E-alone, oestrogen alone; E+P, oestrogen plus progesterone; grad, graduate; HS, high school; HT, hormone therapy; Med visit, visit to a physician within the past year; Meno sympt, history of menopausal symptoms; OS, observational study; P Funct, physical function score from the SF-36; RCT, randomised control trial.

(67.1), limited in climbing stairs (62.8), worse general health (52.1), family history of MI (50.0), lower income (46.4), current history of MI (44.2), white race (44.1), the ratio of waist circumference to hip circumference (38.1), hypertensive medications (33.4), taking calcium channel blockers (24.0) and higher haematocrit (18.6). The C statistic of the predictive value for this equation was high, 0.78 (95% CI 0.77 to 0.79).

Twelve risk factors were independently associated with stroke at the p≤0.0001 level: age (667.4), systolic blood pressure (181.4), history of diabetes (110.3), medication for hypertension (85.3), current smoking (79.9), physical function (68.2), history of stroke (49.1), history of cardiovascular disease (38.8), TIAs (30.8), cardiotonic medication, especially digitalis (27.1), lower income (21.7) and lifetime HT duration (14.9). The C statistics for these variables was 0.76 (95% CI 0.76 to 0.77).

Association of HT with MI and stroke

The risk-adjusted HRs for a specific type of HT (E+P or E-alone) and for either HT are shown in table 2 for each dataset. In the WHI OS dataset E+P and E-alone had similar HRs. In the diet dataset E-alone was significantly protective for MI (HR=0.65) but E+P was not (HR=0.96, p=0.04 for the difference between HRs for E-alone and E+P), and there was no association of either type of HT with stroke. In the RCT datasets there was an association of E+P with an increased risk of MI (HR=1.30) as well as stroke (HR=1.34), but E-alone was not associated with MI.

To test for differences in HRs among the datasets, we combined all datasets and included main effects, interactions between HT and dataset and risk factors in the Cox model. The MI HRs for E+P was larger in the E+P RCT than in the OS (p=0.07), and the MI HR for E-alone was higher in the RCT for E-alone than in the diet dataset (p=0.06). For stroke, where the evidence for the HT risk is stronger, the HR in the combined RCT datasets was significantly higher than it was in the WHI OS dataset (p<0.0001) and in the diet dataset (p=0.005).

Influence of patient characteristics on the association between HT and outcomes

The analyses reported in tables 3 and 4 examined how OS and RCT differences might be influenced by the timing of the HT with respect to age, menopausal status and previous hormones. Also these tables show the effects of additional adjustment for confounding using propensity scores. The HRs and their CIs are presented for women on any HT. Where it might be informative, HRs without CIs are presented for women on a specific type of HT (either E+P or E-alone).

Myocardial infarction

Table 3 presents the MI HR for HT, E+P and E-alone. The timing hypothesis suggests that HRs should be significantly lower in the 50–59 age group or in the group with menopause less than 10 years than in the other groups, but none of these differences were significantly different in the expected direction. To the contrary, the

Table 2 Risk-adjusted HRs for hormone therapy in different datasets

		Myocardial infarction		Stroke	
Dataset	**HT type**	**HR**	**95% CI**	**HR**	**95% CI**
WHI OS	Any E	0.83	(0.72 to 0.95)	0.85	(0.70 to 1.03)
	E+P	0.86*	(0.70 to 1.05)	0.82*	(0.65 to 1.04)
	E-alone	0.80†	(0.69 to 0.94)	0.88‡	(0.71 to 1.11)
Diet RCT	Any E	0.75	(0.62 to 0.89)	1.04	(0.80 to 1.37)
	E+P	0.96	(0.75 to 1.22)	1.00	(0.72 to 1.39)
	E-alone	0.65†§	(0.53 to 0.81)	1.07	(0.79 to 1.45)
HT RCT	Any E	1.18	(0.99 to 1.41)	1.29	(1.05 to 1.58)
	E+P	1.30	(1.02 to 1.65)	1.34	(1.02 to 1.77)
	E-alone	1.05	(0.81 to 1.36)	1.23	(0.91 to 1.67)

*Differs from the comparable RCT HR at the p<0.01 level.
†Differs from the comparable RCT HR at the p=0.02 level.
‡Differs from the comparable RCT HR at the p=0.06 level.
§Differs from 1.00 at the p<0.0001 level.
Any E, E+P or E-alone; E-alone, oestrogen alone; E+P, oestrogen plus progesterone; HT, hormone therapy; OS, observational study; RCT, randomised controlled trial; WHI, Women's Health Initiative.

E+P HR for women aged 50–59 was much higher (1.63) than it was for older women (1.01 for women age 60–69).

The HR for HT during the first 3 years (1.26) is greater than the subsequent risk (1.08). For the RCT for E+P the difference is greater, 1.45 vs 1.11, and the test of the time-dependent covariables of duration of exposure was of marginal statistical significance (p<0.05). Since OS participants on HT began HT several years before enrolment, a diminished effect of HT with time could explain an OS/RCT difference. However, results of other analyses do not support this explanation: there was no evidence that previous HT exposure reduced the HR in the RCT (ie, the HR was lower for participants with no previous exposure, 1.07, than for those with previous exposure, 1.51), and there was no indication in the WHI OS dataset of increased MI risk for participants who began HT after study baseline, the HR was lower than it was for participants who began HT at baseline. (Information on HT usage after baseline was not available for the diet RCT study.)

The last rows in table 3 are HRs stratified by propensity scores. Stratifying by propensity score in addition to adjusting for the significant covariables was expected to reduce confounding, but there was no evidence that doing this gave results similar to the RCTs.

Additional factors that significantly modulated the association between HT and MI in the OS dataset at the p<0.05 level included blood pressure, previous coronary revascularisation, hours of sleep, haematocrit, working status, thyroid disease, antineoplastics, private medical insurance, bone fracture after age 55, colon polyps, ever lived or worked on farm and hostility. Neither education nor income was a statistically significant modulating variable. No factors that significantly modulated the HT HR in the WHI OS dataset also significantly modulated this HR in the RCT datasets. The MI HRs in the RCT and OS datasets did not become similar if they were stratified by the modulating variables.

Stroke

Although E+P and E-alone had similar associations for stroke, results in table 4 include only the HRs for HT and no HRs for E+P and E-alone. As shown in this table there was no consistent evidence that the HT HR for stroke was lower for women who were younger or had menopause recently. In contrast to the MI analyses, there was also no RCT evidence that the HT HR for stroke was stronger soon after beginning HT.

The only variable found to significantly influence HT HR for stroke in the WHI OS dataset was endometrial aspiration; the HR was 0.85 for those who had had an endometrial aspiration and 1.16 for participants who did not (p<0.001). Stratifying on this variable did not make the OS and RCT results more similar. In addition, the lack of an obvious medical explanation, the number of factors tested and the lack of this relationship in the RCT datasets makes it more likely that this result occurred by chance.

After recalculating the HR in the WHI OS dataset for only those participants with midrange of propensity scores (those with a probability of using HT between 0.25 and 0.75), the HR for stroke was virtually unchanged. This suggests that adjusting for the propensity score did not diminish confounding.

Adequacy of WHI information to eliminate confounding

In table 5, the MI risks are compared for participants in the four different WHI datasets who are on the same treatment at baseline (E+P, E-alone or no HT). The HR in the table represents the risk of the outcome for participants in that dataset compared with participants on the same treatment in the WHI OS dataset. If the WHI variables are adequate to eliminate confounding, the adjusted HRs should be near 1.00.

Some HRs shown in the table were statistically significant at p<0.0001. For participants not taking HT the risk-adjusted HR was 1.37 for the RCT for E-alone. For

Table 3 MI HRs for hormone therapy in subgroups defined by participant characteristics associated with hormone exposure

Subgroup within dataset	Dataset					
	RCTs for HT		RCT for diet		WHI OS	
	MI HR for HT in the subgroup of the indicated dataset (Numbers in parentheses are HRs for E+P and E-alone)					
		95% CI		95% CI		95% CI
All participants	1.18 (1.30,1.05)	0.99 to 1.41	0.75 (0.95,0.65)	0.62 to 0.89	0.83 (0.86, 0.80)	0.72 to 0.95
Age						
50–59	1.25 (1.63,0.69)	0.80 to 1.96	0.57 (0.73,0.44)	0.37 to 0.89	0.73 (0.74,0.60)	0.54 to 0.99
60–69	1.01 (1.05,0.95)	0.78 to 1.32	0.73 (0.88,0.65)	0.56 to 0.94	0.87 (0.97,0.81)	0.71 to 1.07
70–79	1.46 (1.46,1.20)	0.99 to 2.15	0.87 (1.33,0.74)	0.65 to 1.18	0.84 (0.75,0.86)	0.68 to 1.03
Years since meno						
<10	1.03 (1.14,0.77)	0.73 to 1.46	0.83 (1.01,0.68)	0.60 to 1.15	0.85 (0.94,0.80)	0.73 to 0.99
10–19	0.95 (1.06,0.74)	0.68 to 1.34	0.67 (0.95,0.47)	0.48 to 0.95	0.77 (0.74,0.72)	0.44 to1.35
>19	1.41 (1.77,1.23)	1.08 to 1.85	0.69 (0.60,0.70)	0.50 to 0.93	1.35 (0.61,1.28)	0.46 to 3.96
HT after baseline			No data		0.71 (0.76, 0.72)	0.57 to 0.88
Follow-up for RCT						
End 3 years after enrolment	1.26 (1.45,1.06)	1.00 to 1.58			0.86 (0.87,0.85)	0.71 to 1.02
Begin 3 years after enrolment	1.08 (1.11,1.04)	0.82 to 1.41			0.79 (0.84,0.73)	0.64 to 0.97
Previous use of HT						
No	1.07 (0.96,1.20)	0.86 to 1.32				
Yes	1.51 (1.12,1.46)	1.09 to 2.08				
Propensity score						
<0.25	1.26 (1.27,1.18)	0.96 to 1.66	0.75 (0.76, 0.71)	0.48 to 1.17	0.98 (1.04,0.83)	0.72 to 1.34
0.25–0.75	1.11 (1.32,1.02)	0.87 to 1.42	0.80 (1.01, 0.69)	0.64 to 1.00	0.85 (0.81, 0.86)	0.72 to 1.01
>0.75	1.05 (NA, 0.93)	0.42 to 2.64	0.69 (1.08, 0.67)	0.34 to 1.40	0.76 (0.96, 0.74)	0.45 to 1.27

E-alone, oestrogen alone; E+P, oestrogen plus progestin; HT, hormone therapy; meno, menopause; MI, myocardial infarction; NA, not available because only one MI case in this group; OS, observational study; RCT, randomised controlled trial; WHI, Women's Health Initiative.

Table 4 Stroke HRs for hormone therapy in subgroups defined by participant characteristics associated with hormone exposure

Subgroup within dataset	Dataset					
	RCTs for HT		RCT for diet		WHI OS	
	Stroke HR for HT in the subgroup of the indicated dataset					
		95% CI		95% CI		95% CI
All patients, full follow-up	1.29	(1.05, 1.58)	1.04	(0.80, 1.37)	0.85	(0.70, 1.03)
Age						
50–59	1.03	0.59 to 1.82	0.48	(0.24, 0.98)	1.04	0.61 to 1.78
60–69	1.65	1.20 to 2.27	1.33	0.90, 1.96	0.96	0.71 to 1.29
70–79	1.11	0.81 to 1.51	1.14	0.74, 1.77	0.75	0.55 to 1.01
Years since menopause						
<10	1.33	0.87 to 2.05	0.85	0.52, 1.40	0.79	0.62 to 1.00
10–19	1.4	0.96 to 2.06	1.05	0.61, 1.82	0.67	0.39 to 1.17
≥20	1.22	0.91 to 1.63	1.21	0.81, 1.80	0.93	0.38 to 2.27
Follow-up for RCT						
End 3 years after enrolment	1.33	1.02 to 1.73			0.75	0.58 to 0.98
Begin 3 years after enrolment	1.26	0.92 to 1.74			0.96	0.72 to 1.27
Previous use of HT						
No	1.33	1.03 to 1.72				
Yes	1.21	0.86 to 1.71				
Propensity scores					0.88	0.70 to 1.12
<0.25	1.18	0.86 to 1.63	0.80	0.41 to 1.55	0.91	0.59 to 1.42
0.25–0.75	1.34	1.02 to 1.76	1.30	0.95 to 1.79	0.88	0.70 to 1.12
>0.75	2.57	0.78 to 8.43	0.50	0.19 to 1.32	0.79	0.41 to 1.51

HT, hormonal therapy; OS, observational study; RCT, randomised controlled trial; WHI, Women's Health Initiative.

participants taking E-alone the HR in the RCT was 1.44, and for participants taking E+P the HR was 1.53 for intervention participants. Risk-adjustment sometimes made HRs closer to 1.00 as expected (eg, intervention participants in the RCT for E+P), sometimes had minimal effect on HRs, and sometimes made a non-significant HR significant (eg, participants not on HT in the diet dataset).

Table 5 MI HRs comparing participants in each of the three RCT datasets to WHI OS participants

Outcome	Dataset	Unadjusted HR	Unadjusted χ^2	Adjusted† HR	Adjusted† χ^2
Patients not on HT (N=78 069)					
	RCT E+P	0.97	0.15	1.20	6.14
	RCT E alone	1.43***	24.98	1.37***	18.69
	RCT diet	1.01	0.07	1.14**	7.08
Patients on E+P (N=35 021)					
	RCT E+P	2.43***	97.23	1.53***	19.08
	RCT diet	1.29*	5.97	1.37**	8.86
Patients on E-only (N=38 672)					
	RCT E only	1.89***	58.17	1.44***	17.23
	RCT diet	0.99	0.00	1.04	0.22

*p<0.05.
**p<0.01.
***p<0.0001.
†Covariables used for the adjustment are described in the text.
E+P, oestrogen plus progestin; HT, hormone therapy; MI, myocardial infarction; OS, observational study; RCT, randomised controlled trial; WHI, Women's Health Initiative.

DISCUSSION

The WHI data analysed contained information on more than 800 possible confounders including information that made it possible to accurately predict HT use. It also contained information on factors that might have influenced response to HT. Some of these factors were related to the timing hypothesis (eg, age, time since menopause, previous HT use, beginning HT after baseline), and some were identified empirically (eg, blood pressure, previous coronary revascularisation and private medical insurance). Since OS and RCT participants differed with respect to these factors, these factors could have conceivably contributed to differences between the OSs and the RCTs. However, after taking into account all of these confounding factors and stratifying on factors that may have influenced the response to HT, OS and RCT differences remained.

The WHI data also contained information from four different studies, and the participants in these studies had different outcomes. After stratifying participants with respect to the type of HT and taking into account the information available in the WHI, we could not eliminate the outcome differences from the four studies.

The above results suggest that there were important risk factors not captured by the WHI that contributed to confounding. Since the WHI dataset is unusually comprehensive, it is likely that most OSs do not capture information on these risk factors. Without including information on potentially important confounders OSs cannot give reliably valid results.

Comparison to previous studies

OSs prior to WHI suggested a 30–50% reduction in coronary heart disease incidence among women using HT.[6–8] There was a smaller benefit shown in the analyses of the observational data in the present study: a 17% reduction in the OS and a 25% reduction in the RCT for diet.

After the WHI results were published, six studies of the association between HT and stroke or MI compared RCT results from the WHI with observational study results: three of these studies used observational data from the WHI[13 15 16] and three used observational data from the Nurses' Health Study.[9 10 14] Two of the WHI studies found, after controlling for time on HT and covariables, E+P HRs for MI did not significantly differ for the two study designs but HRs for stroke were higher in the RCT.

The goals and analytic methods of the present study differ substantially from previous studies using WHI data. The lead author believed that the extensive WHI data would be sufficient to give reliably valid results and extraordinary efforts were made to confirm this hypothesis. These efforts included an assessment of more than 800 risk factors as potential confounders and evaluating all marginally significant or previously suggested factors as potential effect modifiers. Even when the OS and RCT results were not the same, it was possible that the OS results were still valid. As a more definitive test of the adequacy of the WHI data we tried to eliminate differences in risk-adjusted outcomes from different datasets, which few if any other studies have attempted.

The present study differed from previous WHI studies in the following ways: (1) it included participants with and without a uterus, which made it possible to assess the effect of HT preparation. (2) It included participants in the diet RCT, which made it possible to compare risk-adjusted outcomes for two RCT and two OS datasets. (3) It evaluated more than 800 possible risk factors including those often suspected to cause confounding such as socioeconomic status, health behaviours, life style, stress and psychological characteristics. (4) It screened numerous participant characteristics for possible modulating effects on the association between HT and outcomes. (5) It analysed the risk for OS participants who began taking HT after enrolment. (6) It compared participants on the same treatment in different datasets and demonstrated that adjusting for WHI variables does not necessarily eliminate risk differences between datasets.

One of the WHI studies previously evaluated the timing hypothesis and did not find effects of prior HT use or menopause within 5 years.[16] Another analysis of WHI data has been often cited as supporting the timing hypothesis.[17] Although we tried to define coronary heart disease and years since menopause to get the same results, we could not. This suggests that the trends in the previous analysis were not robust to changing definitions.

A WHI study also found, as we did in the present study that the MI HR for E+P was greatest in the early years of treatment. This could explain OS and RCT differences because most OS participants taking HT at baseline began HT several years prior to baseline. However, some analyses in the present study did not support this explanation: (1) the RCT did not find that the effect of E-alone on MI changed over time; (2) none of the datasets found that the effect of any HT on stroke changed over time; (3) WHI OS participants who began HT after baseline had low MI risk and (4) prior HT exposure did not reduce the association between HT and cardiovascular disease.

Results from the OS performed by the Nurses' Health Study differed from our analysis of the WHI OS in important respects. One was that there was no protective association of HT and CHD for women over the age of 60.[9] (Other studies have also suggested that HT is less protective for older women.[11 12]) A second was that there was increased risk for new initiators of HT during the first 2 years after initiation and the risk increased 10 years after menopause.[14] Based on these findings the researchers in the Nurses' Health Study hypothesised that the OS results might be influenced by timing of HT initiation in relation to menopause onset or age and by length of follow-up. A third result that differed from ours was that HT significantly increased the risk of stroke.[10] Since this later result was similar to the WHI RCTs and the previous results might have explained differences between OSs and RCTs, the Nurses' Health Study suggested that OSs of HT could get the same results as RCTs.

The disagreements between our results and the results of the Nurses' Study do not show that the analyses or interpretation in either study are necessarily incorrect. The disagreements do demonstrate, however, the difficulty of getting valid results from OSs.

In addition to OSs of the Nurses' Health Study that give results similar to RCTs there is also an RCT that found oestradiol had an extraordinary protective effect on cardiovascular disease, which is consistent with the weaker protective effect of a different oestrogen preparation in the WHI OS.[12]

A previously published analysis of the WHI data shows that WHI risk factors cannot eliminate the association of adherence to placebo with MI, stroke or breast cancer.[18] Since the effect of adherence to placebo is probably a marker of unmeasured confounders, that study supports the implication of the present study that WHI risk factors are inadequate to eliminate unmeasured confounders.

Limitations

This study provided strong evidence that the WHI did not collect information on important risk factors related to MI or stroke. Although the WHI is unusually comprehensive, other datasets may provide information about these risk factors or about the risk factors that could

cause confounding for the outcomes they assessed. It is also possible that the WHI did collect the necessary information on the confounding factors, but the analytic methods used here were inadequate to take advantage of this information. However, the concerns raised by this study are still valid because both the dataset and the analytic methods used were much more comprehensive than is practical for almost all OSs.

Conclusion and future directions

We did not find that the comprehensive data provided by the WHI were adequate to overcome problems often attributed to OSs. The findings do not imply that most OSs are invalid. They do suggest, however, that given the current methodology, even very good OS datasets may not be adequate to give reliably valid results.

Owing to the key role that OSs are likely to play in studies of comparative effectiveness, it is critical to find ways to make OSs more valid. Although there has been some research on OS methodology,[14] more is required. There should be investigations to learn why some OSs agree with RCTs and others do not. More specific research goals include the following: (1) identify criteria for treatments unlikely to have confounding problems (eg, when there is little patient input to treatment, and one treatment is not preferred for higher risk patients), (2) find new risk factors that better adjust for patient behaviours that affect outcomes (eg, factors related to choosing or adhering to treatment) and (3) develop methods for assessment of confounding after data collection (eg, finding good markers for important unmeasured confounding factors). Without better OS methodology there will be underuse or misuse of OSs for comparative effectiveness research.

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REFERENCES

1. Feinstein AR. Epidemiologic analyses of causation: the unlearned scientific lessons of randomized trials. *J Clin Epidemiol* 1989;42:481–9. discussion 99–502.
2. Moses LE. Measuring effects without randomized trials? Options, problems, challenges. *Med Care* 1995;33(4 Suppl):AS8–14.
3. Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. *N Engl J Med* 2000;342:1878–86.
4. Investigators WGftWsHI. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. *JAMA* 2002;288:321–33.
5. Anderson GL, Limacher M, Assaf AR, *et al*. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004;291:1701–12.
6. Barrett-Connor E, Grady D. Hormone replacement therapy, heart disease, and other considerations. *Annu Rev Public Health* 1998;19:55–72
7. Grady D, Rubin SM, Petitti DB, *et al*. Hormone therapy to prevent disease and prolong life in postmenopausal women. *Ann Intern Med* 1992;117:1016–37.
8. Stampfer MJ, Colditz GA. Estrogen replacement therapy and coronary heart disease: a quantitative assessment of the epidemiologic evidence. *Prev Med* 1991;20:47–63
9. Grodstein F, Manson JE, Stampfer MJ. Hormone therapy and coronary heart disease: the role of time since menopause and age at hormone initiation. *J Womens Health (Larchmt)* 2006;15:35–44
10. Grodstein F, Manson JE, Stampfer MJ, *et al*. Postmenopausal hormone therapy and stroke: role of time since menopause and age at initiation of hormone therapy. *Arch Intern Med* 2008;168:861–6.
11. Salpeter SR, Cheng J, Thabane L, *et al*. Bayesian meta-analysis of hormone therapy and mortality in younger postmenopausal women. *Am J Med* 2009;122:1016–22. e1.
12. Schierbeck LL, Rejnmark L, Tofteng CL, *et al*. Effect of hormone replacement therapy on cardiovascular events in recently postmenopausal women: randomised trial. *BMJ* 2012;345:e6409.
13. Prentice RL, Langer RD, Stefanick ML, *et al*. Combined analysis of Women's Health Initiative observational and clinical trial data on postmenopausal hormone treatment and cardiovascular disease. *Am J Epidemiol* 2006;163:589–99.
14. Hernan MA, Alonso A, Logan R, *et al*. Observational studies analyzed like randomized experiments: an application to postmenopausal hormone therapy and coronary heart disease. *Epidemiology* 2008;19:766–79.
15. Prentice RL, Langer R, Stefanick ML, *et al*. Combined postmenopausal hormone therapy and cardiovascular disease: toward resolving the discrepancy between observational studies and the Women's Health Initiative clinical trial. *Am J Epidemiol* 2005;162:404–14.
16. Prentice RL, Manson JE, Langer RD, *et al*. Benefits and risks of postmenopausal hormone therapy when it is initiated soon after menopause. *Am J Epidemiol* 2009;170:12–23.
17. Rossouw JE, Prentice RL, Manson JE, *et al*. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. *JAMA* 2007;297:1465–77.
18. Hartz A, He T. Why is greater medication adherence associated with better outcomes. *Emerg Themes Epidemiol* 2013. Published Online 2 Feb 2013. doi:10.1186/1742-7622-10-1

Total 869 variables

Form 2 Eligibility Screening (45)

Variable	Label
AGEHYST	Hysterectomy age group
AVAILDM	Available for regular dietary meetings
AVAILHRT	Consider taking only HRT from CC
BLDPROB	Bleeding problem ever
CHF_F2	Heart failure ever
COMECC	Able to come to clinic
DBDIETF2	Special diet for diabetes
DIAB	Diabetes ever
DIABAGE	Age first told had diabetes
DIABCOMA	Hospitalized for a diabetic coma
DIABNW	Diabetes now
DIABPILL	Pills for diabetes ever
DIABTRT	Diabetes treated (pills or shots)
DIALYSIS	Kidney dialysis for kidney failure
DVT_F2	DVT ever
HARDSTDY	Problems make it hard to participate
HELPCC	Kind of help needed to come to clinic
HELPFILL	Need someone to help fill out forms
HORM	Female hormones ever
HORM3M	Female hormones last 3 months
HORMBK	Hormones to treat osteoporosis fracture
HORMSTAT	HRT use ever
HRTINFDR	Send HRT info to Doctor
HYST_F2	Hysterectomy ever
HYST3M	Hysterectomy last 3 months
HYSTAGE	Age at hysterectomy
INSULIN	Insulin shots ever
INSULINW	Insulin shots now
INTDM	Interested in DM part of study
INTHRT_F2	Interested in HRT part of study
L15LBS6M	Lost 15 lbs in the last 6 mo w/o trying
LFDIETF2	Special low-fiber diet
LIVERDIS	Liver disease ever
MALDIET	Special malabsorption diet
MEALOUT	10 or more meals prepared away from home
MENSELST	Last time had any menstrual bleeding
MI_F2	MI ever
MIAGE	Age first had MI
OSTEOBK	Osteoporosis-related fracture ever
OTHCHRON	Other long-term illness
PE_F2	Pulmonary embolism ever

SCANEMIA	Sickle cell anemia ever
STROKE_F2	Stroke ever
TALKDOC	Interested in talking to Dr. about HRT
TIA_F2	TIA ever

Form 20 Personal Information (47)

Variable	Label
ABNPAP3Y	Abnormal Pap smear last 3 years
ANYINS	Any Insurance
CAREPROV	Current Health Care Provider
CERVDYS	Cervical dysplasia ever
DISABLED	Currently disabled
EMPLOYED	Currently employed (full- or part-time)
ENDOASP	Endometrial aspiration ever
HMOINS	Pre-paid private insurance
HOMEMKR	Currently homemaker
INCOME	Family Income
JOBHMMKR	Job as homemaker
JOBLABOR	Job as operator, fabricator, laborer
JOBMANGR	Job as managerial, professional
JOBOTH	Job as other than listed
JOBSERV	Job as service
JOBTECH	Job as technical, sales, admin support
LSTASPDY	Days from rand to last aspiration
LSTMAMDY	Days from rand to last mammogram
LSTPAPDY	Days from rand to last pap smear
LSTVISDY	Days from rand to last visit
MAINJOB	Occupation
MAMMO	Mammogram ever
MARITAL	Marital status
MEDICAID	Medicaid
MEDICARE	Medicare
MLTRYINS	Military or VA insurance
NOINS	No insurance
NOMAM2YR	No mammogram in last 2 years
NOPAP3YR	No pap smear in last 3 years
NOTWRK	Currently not working
OTHPRVIN	Private insurance (other than pre-paid)
OTHWRK	Other current job status
PAPSMEAR	Pap smear ever
PAYOTH	Other insurance than listed
PDISABLE	Partner currently disabled
PEDUC	Partner highest level of education
PEMPLOY	Partner currently employed

PHOMEMKR	Partner currently homemaker
PMAINJOB	Partner's main job
PNOTWRK	Partner currently not working
POTHWRK	Partner currently other job
PRETIRED	Partner currently retired
RETIRED	Currently retired
TIMELAST	Time Since Last Medical Visit (months)
TIMELSTS	Last Medical Visit within 1 Year
USSERVE	Served in US armed forces
VAMEDCTR	Used a VA medical center ever

Form 30 Medical History (95)

Variable	Label
ALS	ALS ever
ALZHEIM	Alzheimer's disease ever
ANGINA	Angina ever
ANGNPILN	Pills for angina now
AORTICAN	Aortic aneurysm ever
ARTHRIT	Arthritis ever
ASTHMA	Asthma ever
ATRIALFB	Atrial fibrillation ever
BKBACK	Broke spine ever
BKBACK55	Broke spine first time 55 or older
BKBONE	Broke bone ever
BKFOOT	Broke foot ever
BKFOOT55	Broke foot first time 55 or older
BKHAND	Broke hand ever
BKHAND55	Broke hand first time 55 or older
BKHIP	Broke hip ever
BKHIP55	Broke hip first time 55 or older
BKLARM	Broke lower arm ever
BKLARM55	Broke lower arm first time 55 or older
BKLLEG	Broke lower leg ever
BKLLEG55	Broke lower leg first time 55 or older
BKOTHB	Broke other bone ever
BKOTHB55	Broke other bone first time 55 or older
BKUARM	Broke upper arm ever
BKUARM55	Broke upper arm first time 55 or older
BLADCA	Bladder cancer ever
BRCA_F30	Breast cancer ever
BRCA55	Breast cancer 55 or older
CABG	Coronary bypass surgery ever
CANC_F30	Cancer ever
CARDCATH	Cardiac catheterization ever

CARDREST	Cardiac arrest ever
CAROTID	Carotid endarterectomy/angioplasty ever
CATARACT	Cataract ever
CERVCA	Cervix cancer ever
CHF_F30	Congestive heart failure ever
COLITIS	Ulcerative colitis ever
COLN_F30	Colorectal cancer ever
COLNSCDT	Date of last colonoscopy
COLNSCPY	Colonoscopy ever
COLOCA55	Colorectal cancer 55 or older
CVD	Cardiovascular disease ever
DIVERTIC	Diverticulitis ever
EMPHYSEM	Emphysema ever
FAINTED	Fainted last 12 months
FRACT55	Fracture at Age 55+
GALLBLRM	Gallbladder removed
GALLBS	Gallbladder disease or gallstones ever
GALLBSNW	Gallbladder disease or gallstones now
GALLSTRM	Gallstones removed
GLAUCOMA	Glaucoma ever
GOITER	Goiter ever
GOITERNW	Goiter now
HEMOCCDT	Date of last hemoccult test
HEMOCCUL	Hemoccult test ever
HIBLDCA	High blood calcium
HICHOLRP	High cholesterol requiring pills ever
HIP55	Hip fracture age 55 or older
HIPREP	Hip replacement ever
HTNTRT	Hypertension
HYPT	Hypertension ever
HYPTAGE	Age told of hypertension
HYPTPILL	Pills for hypertension ever
HYPTPILN	Pills for hypertension now
INTESTRM	Part of intestines removed ever
KIDNEYST	Kidney or bladder stones ever
LUPUS	Lupus ever
MELN_F30	Melanoma cancer ever
MIGRAINE	Migraine headaches ever
MS	MS ever
NACOND	None of listed medical conditions ever
NACVD	None of the listed CVD conditions ever
NODULE	Thyroid nodule ever
NODULENW	Thyroid nodule now
NUMFALLS	Times fell down last 12 months
OTHERCA	Other cancers ever

OTHJREP	Other joint replacement ever
OVRTHY	Overactive thyroid ever
OVRTHYNW	Overactive thyroid now
PAD	Peripheral arterial disease ever
PADANGGR	Angiography for PAD ever
PADANGP	Angioplasty for PAD ever
PADSURG	Surgery to improve flow to legs for PAD
PANCREAT	Pancreatitis ever
PARKINS	Parkinson's disease ever
PCOLONRM	Polyps of colon removed
PTCA	Angioplasty of coronary arteries ever
REVASC	CABG/PTCA Ever
RHEUMAT	Rheumatoid arthritis ever
SKINCA	Skin cancer (not melanoma) ever
STOMULCR	Stomach of duodenal ulcer ever
THYRCA55	Thyroid cancer 55 or older
THYROID	Thyroid Cancer
UNDTHY	Underactive thyroid ever
UNDTHYNW	Underactive thyroid now

Form 31 Reproductive History (54)

Variable	Label
AGEFBIR	Age at First Birth
ANYMENSA	Age at last bleeding
BOOPH	Bilateral Oophorectomy
BRSTAUG	Operation to increase breast
BRSTAUGA	How old at breast augmentation
BRSTBION	How many breast biopsies
BRSTDIS	Breast Disease
BRSTFDAF	How old when first breastfed
BRSTFDAL	How old when last breastfed
BRSTFDM	How many months total
BRSTFDMO	Number of months breastfed
BRSTFDN	How many children breastfed
BRSTFEED	Breastfeed at least one month
BRSTIMP	What type of implant
BRSTOPOT	Any other breast operations
BRSTPREM	Removal of part of breast
BRSTREM	Removal of one or both breasts
BRSTREMO	Other breast operation
BRTHSTLN	How many still births
ECTPREG	How many tubal pregnancies
FULLTRMR	Full term pregnancy ever
GRAVID	Number of Pregnancies

MENARCHE	Age at first period
MENOPSEA	Age at last regular period
MENPSYAF	Age at first hot flash
MENPSYAL	Age at last hot flash
MENPSYMP	Hot flashes or night sweats
MENSREG	Were periods regular
MENSREGA	Age at first regular period
MENSWO1Y	One year without period
MENSWOD	Time between first and last period
MISCARYN	How many miscarriages
NEDLASP	Needle aspiration ever
NOCNCEIV	Tried becoming pregnant > 1 yr
NOCNCVDK	Don't know reason
NOCNCVDR	Saw doctor because you didn't
NOCNCVEN	Endometriosis
NOCNCVHR	Hormones or ovulation
NOCNCVOT	Other problem with you
NOCNCVPT	Problem with partner
NOCNCVR	Reason found for non-pregnancy
NOCNCVUT	Tubes or uterus
NUMLIVER	Number of Live Births
OOPH	One or both ovaries removed
OOPHA	Age when ovaries removed
PARITY	Number of Term Pregnancies
PREG	Ever been pregnant
PREG6M	Ever have full-term pregnancy
PREG6MAF	Age at first term pregnancy
PREG6MAL	Age at last term pregnancy
PREG6MN	How many times term pregnancy
PREGNUM	How many times pregnant
TUBTIED	Ever had tubes tied
TUBTIEDA	Age when tubes tied

Form 32 Family History (79)

Variable	Label
BKBCKDAD	Age father broke spine or back
BKBCKMOM	Age mother broke spine or back
BKBONDAD	Father broke a bone after age 40
BKBONMOM	Mother broke a bone after age 40
BKBONREL	Mom or dad broke bone after age 40
BKHIPDAD	Age father broke hip
BKHIPMOM	Age mother broke hip
BKLARDAD	Age father broke lower arm
BKLARMOM	Age mother broke lower arm

BKOTHDAD	Age father broke other than listed bone
BKOTHMOM	Age mother broke other than listed bone
BKUARDAD	Age father broke upper arm
BKUARMOM	Age mother broke upper arm
BRCADAU1	Age daughter (1) had breast cancer
BRCADAU2	Age daughter (2) had breast cancer
BRCADAU3	Age daughter (3) had breast cancer
BRCAFREL	Female relative had breast cancer
BRCAGMAM	Age mat. grandmother had breast cancer
BRCAGMAP	Age pat. grandmother had breast cancer
BRCAMOM	Age mother had breast cancer
BRCASIS1	Age sister (1) had breast cancer
BRCASIS2	Age sister (2) had breast cancer
BRCASIS3	Age sister (3) had breast cancer
BRONUM	Number of brothers
BROTHER	Have a brother who reached adulthood
CANCFREL	Female relative had cancer
CANCMREL	Immediate male blood relative had cancer
CERVREL	Relative had cervical cancer
CERVRELN	Number of relatives had cervical cancer
COLOBRO1	Age brother (1) had colorectal cancer
COLOBRO2	Age brother (2) had colorectal cancer
COLOBRO3	Age brother (3) had colorectal cancer
COLODAD	Age father had colorectal cancer
COLODAU1	Age daughter (1) had colorectal cancer
COLODAU2	Age daughter (2) had colorectal cancer
COLOFREL	Female relative had colorectal cancer
COLOMOM	Age mother had colorectal cancer
COLOMREL	Male relative had colorectal cancer
COLOREL	Male/Female relative had colorectal cancer
COLOSIS1	Age sister (1) had colorectal cancer
COLOSIS2	Age sister (2) had colorectal cancer
COLOSIS3	Age sister (3) had colorectal cancer
COLOSON1	Age son (1) had colorectal cancer
COLOSON2	Age son (2) had colorectal cancer
DADAGE	Natural father's current age
DADALIVE	Natural father still alive
DADDIEDA	Age natural father died
DAUGHTER	Have a daughter who reached adulthood
DAUNUM	Number of daughters
DIABREL	Relative had adult diabetes
DIABRELN	Number of relatives had adult diabetes
ENDOREL	Relative had endometrial cancer
ENDORELN	Number of relatives had endomet. cancer
MIBRO1	Age brother (1) had MI

MIBRO2	Age brother (2) had MI
MIBRO3	Age brother (3) had MI
MIDAD	Age father had MI
MIDAU1	Age daughter (1) had MI
MIDAU2	Age daughter (2) had MI
MIMOM	Age mother had MI
MIREL	Relatives had heart attack
MISIS1	Age sister (1) had MI
MISIS2	Age sister (2) had MI
MISIS3	Age sister (3) had MI
MISON1	Age son (1) had MI
MISON2	Age son (2) had MI
MOMAGE	Natural mother's current age
MOMALIVE	Natural mother still alive
MOMDIEDA	Age natural mother died
OVARREL	Relative had ovarian cancer
OVARRELN	Number of relatives had ovarian cancer
PROSREL	Relative had prostate cancer
PROSRELN	Number of relatives had prostrate cancer
SISNUM	Number of sisters
SISTER	Have a sister who reached adulthood
SON	Have a son who reached adulthood
SONNUM	Number of sons
STRKREL	Relative had a stroke
STRKRELN	Number of relatives who had a stroke

Form 34 Personal Habits (54)

Variable	Label
ALC12DR	Drank 12 alcoholic beverages ever
ALCNOW	Still drink alcohol
ALCOHOL	Alcohol intake
ALCQUIT	Reasons quit drinking alcohol
ALCSWK	Alcohol servings per week
AVWKEXP	Energy expend from avg walking
CIGSDAY	Smoke, cigs/day
COFFEE	Drink coffee each day
CUPREG	Number of regular cups of coffee, day
DBDIET34	Diabetic or ADA diet
FBDIET34	High-fiber diet
FFWKEXP	Energy expend fr walking fairly fast
HARDEXP	Energy expenditure from hard exercise
HRDEX	Times per week of very hard exercise
HRDEX18	Very hard exercise 3 times/wk at age 18
HRDEX35	Very hard exercise 3 times/wk at age 35

HRDEX50	Very hard exercise 3 times/wk at age 50
HRDEXMIN	Duration per time of very hard exercise
LACTDIET	Lactose-free (no milk/dairy foods) diet
LCALDIET	Low calorie diet
LEPITOT	Recr. phys activity per week >= 20 Min
LFATDIET	Low-fat or low cholesterol diet
LMSEPI	Mod-stren activity >20 min/week (categorical)
LSLTDIET	Low salt (low sodium) diet
MILDEXP	Energy expenditure from mild exercise
MLDEX	Times per week of mild exercise
MLDEXMIN	Duration per time of mild exercise
MODEX	Times per week of moderate exercise
MODEXMIN	Duration per time of moderate exercise
MODEXP	Energy expend from moderate exercise
MSEPIWK	Mod. to strenuous phys activity per week
MSMINWK	Minutes of mod-stren activity per week
OTHDIET	Other than listed special diet
QSMOKAGE	Age quit smoking regularly
QSMOKHP	Quit smoking because of health problems
SEPIWK	Strenuous activity episodes per week
SMINWK	Minutes of stren. phys activity per week
SMOKAGE	Age started smoking cigarettes regularly
SMOKEVR	Smoked at least 100 cigarettes ever
SMOKING	Smoking status
SMOKNOW	Smoke cigarettes now
SMOKWGT	Smoked to lose weight
SMOKYRS	Years a regular smoker
TEPIWK	Recreational phys activity per week
TEXPWK	Total MET-hours per week
TMINWK	Minutes of recr. phys activity per week
VFWKEXP	Energy expend from walking very fast
WALK	Times walk for > 10 min
WALKEXP	MET-hours per week from walking
WALKMIN	Duration of walks when >10 min
WALKSPD	Walking speed when walking for >10 min
WGTADULT	Weight during adult life, lbs
XLMSEPI	Mod-stren activity > 20 min/week
YOYO10LB	Number times weight went up/down >10 lbs

Form 37 Thoughts and Feelings (216)

Variable	Label
ACHES	General aches and pains
ACTDLY	Activities of Daily Living Construct
AMBEMOT	Ambivalence over Emotional Expressivenes

ANNOYED	Becoming easily annoyed or irritable
ANXIOUS	Feeling nervous, anxious, on edge
APPRVNEG	Fear others will not approve if negative
BACKSLP	trouble getting back to sleep
BADLUCK	Think people make bad luck for sympathy
BADSEX	People guilty of bad sexual behavior
BATHING	Bathing or dressing yourself
BENDING	Bending, kneeling, stooping
BIRD	Bird
BLOATING	Bloating or gas
BODPAIN	How much body pain
BOTHER	After anger bothered for a long time
CALM	Felt calm and peaceful
CAREGIV1	Care Giving Construct #1 (0,1 scoring)
CAREGIV2	Care Giving Construct #2 (0-5+ scoring)
CAT	Cat
CGHINCON	Leak urine when cough, laugh
CHILCON	Major conflict with children
CLUB	Attend clubs/lodges/groups last month
CLUMSY	Clumsiness
COERCE	Number of people who try to coerce
CONCEN	Difficulty concentrating
CONSTIP	Constipation
COUGH	Coughing or wheezing
COUNTGD	Rarely count on good things happening
CRYSPELL	You had crying spells
DIAPER	Leak protect/Diaper, Attends
DIARRHEA	Diarrhea
DISAPPNT	Express disappointment
DIVORCE	Have a divorce or break-up
DIZZY	Dizziness
DOG	Dog
DRESS	Can you dress and undress self
DWNDUMPS	Felt down in dumps
EAT	Can you eat
EMOLIMIT	Role Limitations Due to Emotional Proble
EMOWELL	Emotional Well-being
ENERFAT	Energy/Fatigue
ENERGY	Had lots of energy
ENJLIF	You enjoyed life
EXCLUDE	Number of people who exclude you
EXPCTBST	Usually expect the best
EXPERTS	Experts often no better than I
FALLSLP	fall asleep during quiet activ
FELTBLUE	Felt downhearted and blue

FELTDEP	You felt depressed
FELTSAD	You felt sad
FISH	Fish
FORGET	Forgetfulness
FRIENDIE	Did a close friend die
FRNDIV	Close friend had a divorce
FRNDSUSE	Make friends because friends are useful
FRNJOB	Close friend lost job
FRQINCON	How often leaked urine
FULLPEP	Did you feel full of pep
FUN	Someone to something fun with
GENHEL	In general, health is
GENHLTH	General Health Construct
GOODADVC	Someone to give good advice
GOODTIME	Someone to have a good time with
HAPPY	Have you been happy
HEADACHE	Headaches or migraines
HEARLOSS	Hearing loss
HEARTBRN	Heartburn
HEARTRAC	Heart racing or skipping beats
HLPCHORS	Someone to help with daily chores
HLPPROB	Someone to help understand a problem
HLPSICK	Helping sick family/friend
HLPSICKT	Times helped sick family/friend
HLTHC1Y	Compare health to 1 year ago
HLTHEXCL	My health is excellent
HLTHWORS	I expect health to get worse
HLTHYANY	I am as healthy as anybody
HONEST	Most people are honest due to fear
HOPEFUL	Always hopeful about future
HOSTIL	Hostility Construct
HOTFLASH	Hot flashes
HRSSLP	How many hours of sleep
HUNGRY	Increased appetite
INCONDIS	How much does leakage bother
INCONLMT	leak limit activities
INCONT	Ever leaked urine
INOUTBED	Can you get in and out of bed
INTSOC	Phys or emotional probs interfere
INTSOC2	Physical or emotional problem
JNTPAIN	Joint pain or stiffness
KNWANGRY	Usually people around know when angry
LEAKAMT	How much urine you lose
LESSACCE	Emot/Accomplished less
LESSACCP	Phys/Accomplished less

LESSCARE	Emot/Worked less carefully
LESSKNDP	Phys/limited kind of work
LESSWRKE	Emot/cut down on time spent
LESSWRKP	Phys/cut down on time spent
LFEVENT1	Life Event Construct #1 (0,1 scoring)
LFEVENT2	Life Event Construct #2 (0-3 scoring)
LIE	Most people would lie to get ahead
LIFEQUAL	Rate quality of life
LIFTGROC	Lifting or carrying groceries
LISTEN	Someone to listen when need to talk
LIVALN	Live alone
LIVALOR	Living Alone
LIVCHLD	Live with children
LIVFRNDS	Live with friends
LIVOTH	Live with other than listed
LIVPRT	Live with husband/partner
LIVREL	Live with relatives
LIVSIBL	Live with brother/sister
LOVE	Someone to love you/make you feel wanted
LOWBACKP	Low back pain
MAJACC	Major accident or disaster
MARRIED	Currently married or intimate
MEDSLEEP	take medication for sleep
MENSPAD	Leak Protection/Menstrual pad
MINIPAD	Leak Protect/Mini-pad, tissue
MODACT	Moderate activities
MONPROB	Major problems with money
MOODSWNG	Mood swings
MOREGOOD	Expect more good things than bad
MSCLACHE	Muscle tension aches or soreness
NAP	Did you nap during the day
NAUSEA	Nausea
NECKPAIN	Neck pain
NEGEMOT	Negative Emotional Expressiveness (NEE)
NERVES	Number of people who get on nerves
NERVOUS	Have you been a very nervous person
NIGHTSWT	Night sweats
NOCARE	No one cares what happens to you
NOCONCEN	Trouble concentrating on things, reading
NOHELP	People inwardly don't like to help
NOHUNGER	Decreased appetite
NOINCON	No longer leak urine
NOPRTCT	Leak Protect/No protection
NOTMYWAY	Hardly ever expect things to go my way
OPTIMISM	Optimism Construct

ORDERS	Take orders from someone who knew less
OTHINCON	When leak urine, Other
OTHPET	Other pet
OTHPRTCT	Leaking urine protection, Other
PAIN	Pain Construct
PAININT	How much did pain interfere
PANIC	Having an anxiety attack -- feel fear or panic
PEOPDIS	You felt people disliked you
PET	Lived with a pet in home
PETDIE	Did a pet die
PHYAB	You were physically abused
PHYLIMIT	Role Limitations Due to Physical Health
PHYSFUN	Physical Functioning Construct
PSHTDEP	Shortened CES-D/DIS Screening Instrument
QUALSLP	Typical night's sleep
RELGTIME	Times attend religious service/church
RELSTRN	Religion gives strength and comfort
RESPECT	People demand more respect than give
RESTLSIT	Feeling restless so hard to sit still
RESTSLP	Your sleep was restless
SAD2WK	Felt sad for two weeks
SAD2YRS	Felt sad two or more years
SADMUCH	Felt sad much of past year
SATFRQSX	Satisfied with sex frequency
SATLIFE	Satisfied with quality of life
SATSEX	How satisfied sexually
SCENEPUB	If angered, cause scene in public place
SEX	Who you have had sex with
SEX45	Description of adult sexual orientation
SEXACTIV	Sexual activity in last year
SEXWORRY	Sexual activity affect healh
SHARE	Someone to share private worries/fears
SHOWER	Can you take a bath or shower
SICKEASY	I get sick easier
SKINDRY	Skin dryness or scaling
SLPDSTRB	Sleep Disturbance Construct
SLPINCON	Leak when I am sleeping
SNORE	Did you snore
SOCFUNC	Social Functioning
SOCSTRN	Social Strain Construct
SOCSUPP	Social Support Construct
SPOUSDIE	Did your spouse die
SPOUSILL	Did your spouse have a serious illness
STAIR	Climbing one flight of stairs
STAIRS	Climbing several flights

STAYSLP	Trouble falling asleep or staying asleep
SUPPRESS	Usually suppress anger
SWELLHND	Swelling of hands or feet
SYMPTOM	Symptom Construct
TAKEDR	Someone can take to the doctor
TELLFEEL	Tell from facial expressions how feeling
TIRED	Did you feel tired
TIRED2	Feeling tired
TIREEASY	Getting tired very easily
TOINCON	Leak when can't get to toilet
TOOMUCH	Number of people who ask too much
TRBSEE	Trouble with vision
TRBSLEEP	Did you have trouble sleeping
TREMORS	Tremors
TRUSTNO	Safer to trust nobody
TRUTH	Argue to convince people of truth
UNFAIR	Most people are unfair to gain profit
UPEARLY	wake up earlier than planned
UPSTOM	Upset stomach or belly pain
URINPAIN	Pain/burning while urinating
VAGDIS	Vaginal or genital discharge
VAGDRY	Vaginal or genital dryness
VAGITCH	Vaginal or genital irritation
VERBAB	You were verbally abused
VIGACT	Vigorous activities
WAKENGHT	Did you wake up several times
WALK1BLK	Walking one block
WALK1M	Walking more than one mile
WALKBLKS	Walking several blocks
WELBEING	Rate current sense of well-being
WORNOUT	Did you feel worn out
WRKDIFFP	Phys/difficulty perform work
WRONG	Expect something that can will go wrong

Form 43 Hormone Use (44)

Variable	Label
DES	DES (diethylstilbestrol) use ever
DESAGEMAX	Age stopped DES
DESAGEMIN	Age started DES
DESTIME	DES Duration (years)
DMPA	DMPA (depo-provera) use ever
DMPAFREQ	DMPA frequency of use
DMPAGEMAX	Age last used DMPA
DMPAGEMIN	Age first used DMPA

DMPATIME	DMPA duration (years)
DMPAUOM	DMPA frequency UOM
ESTR	Estratest use
ESTRMAX	Age last used estratest
ESTRMIN	Age first used estratest
ESTRSTAT	Estratest usage status
ESTRTIME	Estratest duration
OC	Oral contraceptive use ever
OCAGEMAX	Age last used OC
OCAGEMIN	Age first used OC
OCBPREG	OC use before first term pregancy
OCBPTIME	OC use before first term preg duration (years)
OCTIME	OC duration (years)
PCYCLE	Progesterone cycle during last PERT use
TEST	Testosterone or other male hormone use
TESTMAX	Age last used testosterone
TESTMIN	Age first used testosterone
TESTSTAT	Testosterone or other male hormone status
TESTTIME	Testosterone or other male hormone duratation
TOTE	Unopposed estrogen use ever
TOTECAT	Unopposed estrogen duration by category
TOTEMAX	Age last used unopposed estrogen
TOTEMIN	Age first used unopposed estrogen
TOTESTAT	Unopposed estrogen usage status
TOTETIME	Lifetime unopposed estrogen duration
TOTH	HRT uuse ever
TOTHCAT	HRT duration by category
TOTHMAX	Age last used HRT
TOTHMIN	Age first used HRT
TOTHSTAT	HRT usage status
TOTHTIME	Lifetime HRT duration
TOTP	Estrogen + progesterone use ever
TOTPMAX	Age last used estrogen + progesterone
TOTPMIN	Age first used estrogen + progesterone
TOTPSTAT	Estrogen + progesterone usage status
TOTPTIME	Lifetime estrogen + progest duration

Form 45 Current Supplements (55)

Variable	Label
F45BETA	Supplemental Beta-carotene, mcg
F45BIOT	Supplemental Biotin, mcg
F45CALC	Supplemental Calcium, mg
F45CHROM	Supplemental Chromium, mcg
F45COMBP	Any Combination Pill

F45COPP	Supplemental Copper, mg
F45FOLIC	Supplemental Folic Acid, mcg
F45IRON	Supplemental Iron, mg
F45MAGN	Supplemental Magnesium, mg
F45MANG	Supplemental Manganese, mg
F45MOLYB	Supplemental Molybdenum, mcg
F45MULTI	Multivitamin without Minerals
F45MVMIN	Multivitamin with Minerals
F45NIAC	Supplemental Niacin, mg
F45OTHCM	Other Comb Pill (not multivit/stress)
F45PANTO	Supplemental Pantothenic Acid, mg
F45PHOS	Supplemental Phosphorus, mg
F45POTAS	Supplemental Potassium, mg
F45RETIN	Supplemental Retinol, mcg
F45SELEN	Supplemental Selenium, mcg
F45STRES	Stress Formula Pills
F45VITA	Supplemental Vitamin A, mcg RE
F45VITB1	Supplemental Vitamin B1 (Thiamine), mg
F45VITB2	Supplemental Vitamin B2 (Thiamine), mg
F45VITB6	Supplemental Vitamin B6, mg
F45VITC	Supplemental Vitamin C, mg
F45VITD	Supplemental Vitamin D, mcg
F45VITE	Supplemental Alpha-tocopherol, IU
F45VTB12	Supplemental Vitamin B12, mcg
F45ZINC	Supplemental Zinc, mg
TKBIOT	F45 Taking biotin from single sup
TKCALC	F45 Taking calcium from single sup
TKCHROM	F45 Taking chromium from single sup
TKCOPP	F45 Taking copper from single sup
TKFOLIC	F45 Taking folic acid from single sup
TKIRON	F45 Taking iron from single sup
TKMAGN	F45 Taking magnesium from single sup
TKMANG	F45 Taking manganese from single sup
TKMOLYB	F45 Taking molybdenum from single sup
TKNIAC	F45 Taking niacin from single sup
TKPANTO	F45 Taking pantoth. acid from single sup
TKPHOS	F45 Taking phosphorus from single sup
TKPOTAS	F45 Taking potassium from single sup
TKRETIN	F45 Taking retinol from single sup
TKSELEN	F45 Taking selenium from single sup
TKVITA	F45 Taking vitamin A from single sup
TKVITB1	F45 Taking vitamin B1 from single sup
TKVITB12	F45 Taking vitamin B12 from single sup
TKVITB2	F45 Taking vitamin B2 from single sup
TKVITB6	F45 Taking vitamin B6 from single sup

TKVITC	F45 Taking vitamin C from single sup
TKVITD	F45 Taking vitamin D from single sup
TKVITE	F45 Taking alpha-toco from single sup
TKZINC	F45 Taking zinc from single sup

Form 60 Energy (139)

Variable	Label
F60ACARO	Dietary Alpha-Carotene (mcg)
F60ADSGR	Dietary Added Sugars (g)
F60ALAN	Dietary Alanine (g)
F60ALC	Dietary Alcohol (g)
F60ALCWK	Alcohol servings per week
F60ANMPR	Dietary Animal Protein (g)
F60ARGIN	Dietary Arginine (g)
F60ASH	Dietary Ash (g)
F60ASPRT	Dietary Aspartic Acid (g)
F60ATOCO	Dietary Alpha-Tocopherol (mg)
F60BCRYP	Dietary Beta-Cryptoxanthin (mcg)
F60BETA	Dietary Beta-Carotene (mcg)
F60BIOCHN	Dietary Biochanin A (mg)
F60BTOCO	Dietary Beta-Tocopherol (mg)
F60CAFF	Dietary Caffeine (mg)
F60CALC	Dietary Calcium (mg)
F60CARB	Dietary Total Carbohydrate (g)
F60CBPCT	Percent Calories from Carbohydrates
F60CHOLS	Dietary Cholesterol (mg)
F60COPPR	Dietary Copper (mg)
F60CUMST	Dietary Coumestrol (mg)
F60CYSTN	Dietary Cystine (g)
F60DAIDZ	Dietary Daidzein (mg)
F60DIETGA	Dietary Glycemic Index (using available carbs)
F60DIETGI	Dietary Glycemic Index (using total carbs)
F60DTOCO	Dietary Delta-Tocopherol (mg)
F60ENRGY	Dietary Energy (kcal)
F60ENRGYJ	Dietary Energy (joules)
F60FAT	Dietary Total Fat (g)
F60FIBER	Dietary Fiber (g)
F60FLDEQ	Dietary Folate Equivalents (mcg)
F60FLNAT	Dietary Natural Folate (food folate) (mcg)
F60FLSYN	Dietary Synthetic Folate (folic acid) (mcg)
F60FOLA	Dietary Folacin (mcg)
F60FRMNT	Dietary Formononetin (mg)
F60FRUCT	Dietary Fructose (g)
F60FRUIT	Daily Fruit Consumption (med portion)

F60FTPCT	Percent Calories from Fat
F60GALAC	Dietary Galactose (g)
F60GLAC	Dietary Glycemic Load Based on Available Carb
F60GLUC	Dietary Glucose (g)
F60GLUT	Dietary Glutamic Acid (g)
F60GLYCN	Dietary Glycine (g)
F60GLYCTN	Dietary Glycitein (mg)
F60GNISTN	Dietary Genistein (mg)
F60GRAMS	Dietary Gram Amount
F60GTLC	Dietary Glycemic Load Based on Total Carb
F60GTOCO	Dietary Gamma-Tocopherol (mg)
F60HISTD	Dietary Histidine (g)
F60INSFB	Insoluble Dietary Fiber (g)
F60IRON	Dietary Iron (mg)
F60ISOLE	Dietary Isoleucine (g)
F60LACT	Dietary Lactose (g)
F60LEUCN	Dietary Leucine (g)
F60LUTZX	Dietary Lutein+Zeaxanthin (mcg)
F60LYCO	Dietary Lycopene (mcg)
F60LYSIN	Dietary Lysine (g)
F60MAGN	Dietary Magnesium (mg)
F60MALT	Dietary Maltose (g)
F60MANGN	Dietary Manganese (mg)
F60METH	Dietary 3-Methylhistidine (mg)
F60METHN	Dietary Methionine (g)
F60MF141	Dietary MFA 14:1 (g)
F60MF161	Dietary MFA 16:1 (g)
F60MF181	Dietary MFA 18:1, Oleic Acid (g)
F60MF201	Dietary MFA 20:1 (g)
F60MF221	Dietary MFA 22:1 (g)
F60MFA	Dietary Total MFA (g)
F60MFPCT	Percent Calories from MFA
F60NATOC	Dietary Natural Alpha-Tocopherol (mg)
F60NIACN	Dietary Niacin (mg)
F60NICNEQ	Dietary Niacin Equivalents (mg)
F60OMGA3	Dietary Omega 3 (g)
F60OMGA6	Dietary Omega 6 FA (g)
F60OXALC	Dietary Oxalic Acid (mg)
F60PANTO	Dietary Pantothenic Acid (mg)
F60PECT	Dietary Pectins (g)
F60PF182	Dietary PFA 18:2, Linoleic Acid (g)
F60PF183	Dietary PFA 18:3, Linolenic Acid (g)
F60PF184	Dietary PFA 18:4 (g)
F60PF204	Dietary PFA 20:4 (g)
F60PF205	Dietary PFA 20:5, EPA (g)

F60PF225	Dietary PFA 22:5 (g)
F60PF226	Dietary PFA 22:6, dha (g)
F60PFA	Dietary Total PFA (g)
F60PFPCT	Percent Calories from PFA
F60PHNYL	Dietary Phenylalanine (g)
F60PHOS	Dietary Phosphorous (mg)
F60PHYTC	Dietary Phytic Acid (mg)
F60POTAS	Dietary Potassium (mg)
F60PROLN	Dietary Proline (g)
F60PROT	Dietary Protein (g)
F60PRPCT	Percent Calories from Protein
F60RETIN	Dietary Retinol (mcg)
F60RIBO	Dietary Riboflavin (mg)
F60SELEN	Dietary Selenium (mcg)
F60SERIN	Dietary Serine (g)
F60SF100	Dietary SFA 10:0 (g)
F60SF120	Dietary SFA 12:0 (g)
F60SF140	Dietary SFA 14:0 (g)
F60SF160	Dietary SFA 16:0, Palmitic Acid (g)
F60SF170	Dietary SFA 17:0 (g)
F60SF180	Dietary SFA 18:0, Stearic Acid (g)
F60SF200	Dietary SFA 20:0 (g)
F60SF220	Dietary SFA 22:0 (g)
F60SF40	Dietary SFA 4:0 (g)
F60SF60	Dietary SFA 6:0 (g)
F60SF80	Dietary SFA 8:0 (g)
F60SFA	Dietary Total SFA (g)
F60SFPCT	Percent Calories from SFA
F60SODUM	Dietary Sodium (mg)
F60SOLFB	Water Soluble Dietary Fiber (g)
F60STOCO	Dietary Synthetic Alpha-Tocopherol (mg)
F60STRCH	Dietary Starch (g)
F60SUCR	Dietary Sucrose (g)
F60TF161	Dietary Trans Fatty Acid, 161T (g)
F60TF181	Dietary Trans Fatty Acid, 181T (g)
F60TF182	Dietary Trans Fatty Acid, 182T (g)
F60TFTOT	Dietary Total Trans Fatty Acid (g)
F60THIAM	Dietary Thiamin (mg)
F60THREO	Dietary Threonine (g)
F60TRYPT	Dietary Tryptophan (g)
F60TSUGR	Dietary Total Sugars (g)
F60TYROS	Dietary Tyrosine (g)
F60VALIN	Dietary Valine (g)
F60VB12	Dietary Vitamin B12 (mcg)
F60VEG	Daily Vegetable Consumption (med portion)

F60VEGPR	Dietary Vegetable Protein (g)
F60VITA	Dietary Vitamin A (RAE)
F60VITAIU	Dietary Vitamin A (IU)
F60VITARE	Dietary Vitamin A (mcg RE)
F60VITB6	Dietary Vitamin B6 (mg)
F60VITC	Dietary Vitamin C (mg)
F60VITD	Dietary Vitamin D (mcg)
F60VITE	Dietary Total Alpha-Toc Eq (mg)
F60VITK	Dietary Vitamin K (NDS Value) (mcg)
F60VTEIU	Dietary Vitamin E (IU)
F60WATER	Dietary Water (g)
F60ZINC	Dietary Zinc (mg)

Form 80 and others (41)

Variable	Label
BMICX	BMI Categorical
BMIX	BMIX
DIAS	Diastolic BP
DIASBP1	Diastolic blood pressure (1st reading)
DIASBP2	Diastolic blood pressure (2nd reading)
DIASTOL	Diastolic BP
group21	Antineoplastics
group24	Estrogens
group249930	Estrogen & Progestin
group26	Progestins
group28	THYROID
group32	ANTIANGINAL AGENTS
group33	BETA BLOCKERS
group34	CALCIUM BLOCKERS
group35	ANTIARRHYTHMIC
group36	ANTIHYPERTENSIVE
group37	DIURETICS
group38	PRESSORS
group39	Antihyperlipidemic
group40	MISC. CARDIOVASCULAR
group57	Antianxiety Agents
group58	Antidepressants
group59	Antipsychotics
group60	Hypnotics
group64	ANALGESICS - NONNARCOTIC
group65	ANALGESICS - NARCOTIC
group72	ANTICONVULSANT
HEMATOCR	Hematocrit (%)
HEIGHTX	**Height cm**

HIPX	**Hip circumference cm**
PLATELET	Platelet count (Kcell/ml)
PULSE30	Resting pulse in 30 seconds
SYST	Systolic BP
SYSTBP1	Systolic blood pressure (1st reading)
SYSTBP2	Systolic blood pressure (2nd reading)
SYSTOL	Systolic BP
WAISTX	**Waist circumference cm**
WBC	White blood cell (Kcell/ml)
WEIGHTX	**Weight kg**
WHEXPECT	Waist and Hip measurement expected
WHRX	**Waist hip ratio**