Supplementary Online Content

Mora S, Wegner NK, Cook NR, et al. evaluation of the pooled cohort risk equations for cardiovascular risk prediction in a multiethnic cohort of women: the Women's Health Initiative [published online July 23, 2018]. *JAMA Intern Med*. doi:10.1001/jamainternmed.2018.2875

This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Appendix

Evaluation of the Pooled Cohort Risk Equations for Cardiovascular Risk Prediction in a Multiethnic Cohort of Women: The Women's Health Initiative

Samia Mora, MD, MHS, Nanette K. Wenger, MD, Nancy R. Cook, ScD,
Jingmin Liu, MS, Barbara V. Howard, PhD, Marian C. Limacher, MD,
Simin Liu, MD, ScD, Karen L. Margolis, MD, MPH, Lisa W. Martin, MD,
Nina Paynter, PhD, Paul M Ridker, MD, MPH, Jennifer Robinson, MD, MPH,
Jacques E. Rossouw, MD, Monika M. Safford, MD, JoAnn E. Manson, MD, DrPH

Table of Contents

Supplementary Methods

Study Design

Study participants were drawn from the WHI that included postmenopausal women age 50 to 79 years who were enrolled (1993-1998) at one of 40 WHI clinical centers nationwide into either a clinical trial (CT; N=68,132) or an observational study (OS; N=93,676). The CT was a randomized controlled evaluation of three distinct interventions: postmenopausal hormone therapy (estrogen alone or estrogen plus progestin), a calcium and vitamin D supplement trial, and a low-fat dietary modification trial.[1] Exclusions included predicted survival <3 years or conditions inconsistent with study participation and adherence. At the baseline clinic visit, body weight, height, waist circumference, and blood pressure were measured, and fasting blood samples were obtained. Demographic characteristics, socioeconomic data, smoking, medical history, and self-reported medications were collected using standardized questionnaires. Race and ethnicity were self-reported. In a central laboratory (University of Minnesota) certified by the CDC/NHLBI Lipid Standardization Program, total cholesterol was measured enzymatically, and HDL cholesterol was measured by heparin manganese precipitation[2] or directly (Roche Diagnostics, Indianapolis).

Outcomes Ascertainment

WHI adjudicated events. OS study participants were contacted annually by mail to obtain updates of their medical histories and selected exposure data. [3] CT study participants were followed through regularly scheduled examinations, intermediate 6-month contacts, and annual clinic visits through 2005, and by annual mailings thereafter through 2013. Among our analytic sample, 1.24% participants were lost to follow-up overall, and among women aged 65 and older and enrolled in Medicare, 0.79% were lost to follow-up. Medical records were requested and reviewed. In the WHI, diagnoses of MI were established by physician adjudicators based on review of medical records using standardized forms and definitions,[3] and stroke was adjudicated by trained vascular neurologists using detailed standards. [4] In addition, participants were asked about all hospitalizations, and potential events were identified from these participant self-reports of hospitalizations and selected

(cardiovascular-related) outpatient diagnoses. WHI also ascertained deaths obtained from periodic searches of the NDI, to complement our routine follow-up of reports of deaths by next of kin and postal authorities. The NDI search was submitted through 2013 for WHI participants who were not enrolled in Extension II (2005-2010). Among the 19,995 women in the analytic sample (i.e., in either the risk validation subcohort or treatment eligibility subcohort), and before including the NDI deaths, a total of 1,499 women had first ASCVD events (1,607 first MI, 242 CHD death, and 1,650 first stroke) over a 12-year follow up; NDI captured an additional 46 events in the risk validation set and 17 events to the treatment eligibility set over a 12-year period. Over 10 years of follow-up, a total of 1,236 WHI-adjudicated first ASCVD events (including 35 NDI stroke and CHD deaths) occurred.

Claims-based events. CMS Part A data were obtained for all Medicare fee-for-service beneficiaries who were enrolled in fee-for-service coverage at the time of WHI enrollment through 2013. The *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes for principal or secondary diagnosis were 410.x0 or 410.x1 to define MI,[5] and ICD-9 430.xx, 431.xx, 433.x1, 434.x1, 436.xx to define stroke.[4]

Statistical Analyses

Model calibration and discrimination. Model calibration (i.e. how well the predicted probability from the model agrees with the actual risk observed) was further assessed using the Hosmer-Lemeshow goodness-of-fit test comparing differences between the average predicted 10-year risk with the actual average 10-year observed risks.[6] Model discrimination (i.e. the relative ranking of individuals, such that those who develop an event during the follow-up period have a higher predicted risk than those who do not develop an event) was evaluated using the c-index,[7] a generalization of the area under the receiver operator characteristic curve that is applicable to survival data.

Analyses that excluded women randomized to the active hormone therapy (HT) arm. HT modifies lipid levels, blood pressure, other vascular risk factors, and subsequent risk of ASCVD. Since baseline risk factor assessment may not reflect ASCVD risk during follow-up for women in the active HT arm, we pre-specified conducting

analyses with and without these randomized participants. As a sensitivity analysis, we also analyzed event rates in the subgroup of women randomized to the placebo arm of the hormone therapy CT (Table S4b).

Accounting for change in statin or aspirin use during follow-up. Using a life table analysis, we increased the rate of ASCVD proportionately among those using statins or aspirin. Since statins have been found in meta-analyses to decrease risk by approximately 25%, we increased the observed risk by 1/0.75 = 1.33 over time among those who were initiated on statin therapy after the baseline visit and lipid assessment (ie. during follow-up) in each time window where statin use was reported (at year 3 for OS participants, and at years 1, 3, 6 and 9 for CT participants.[8] Likewise, as aspirin decreases ASCVD risk by approximately 12%, we increased the observed risk by 1/0.88 = 1.14 over time among those treated with aspirin after the baseline visit (ie during follow-up) in each time window where aspirin use was reported.[9]

Accounting for events ascertained from Medicare claims in women 65 years and older. To assess the impact of more complete outcome ascertainment on the observed risks, we also pre-specified an analysis to incorporate the CMS claims outcomes data that was available on participants aged ≥65 years at study entry who were enrolled in traditional fee-for-service Medicare Part A or A/B coverage as previously described.[4, 5] CMS claims were collected from 1993 to 2013. The ASCVD events analyzed in this group included events adjudicated from medical records in WHI (including 20 NDI deaths), or events detected in Medicare claims data based on discharge diagnosis codes. First, we excluded ASCVD cases that were identified by CMS and had sufficient medical records to be adjudicated by WHI to be non-events. We included both primary and secondary diagnosis claims events in order to be consistent with prior studies which resulted in an additional 65 MIs and 99 strokes. All but 13 of these additional cases were principal (primary) discharge diagnosis claims events. We then multiplied the remaining observed Medicare claims events by a factor of 0.85 (Table S4), consistent with the positive predictive value (PPV) for principal and secondary claims events based on prior WHI analyses that compared Medicare claims with WHI-adjudicated events.[4, 5] Participants were censored when an ASCVD event or death occurred, when surveillance was no longer complete (ie lost to follow-up in WHI or no longer enrolled in Medicare A or A/B), or at end of follow-up. Because PPVs may be lower among those who do not self-report an outcome, in a sensitivity analysis, we only included CMS principal diagnosis claims events and assumed a lower PPV of 0.60 (Table S4).

Table S1a. Race/ethnicity distribution and age distribution before and after weighting to the racial/ethnic and age distribution of the overall WHI cohort

Variable	Overall WHI	Risk Validation Subcohort	Treatment Eligibility Subcohort	Distribution after weighting	
				Risk Validation Subcohort	Treatment Eligibility Subcohort
Race/ethnicity					
White	133,541 (82.5%)	8,151 (41.6%)	5,484 (40.8%)	82.5%	82.5%
Black	14,618 (9.0%)	7,492 (38.3%)	5,035 (37.5%)	9.0%	9.0%
Hispanic	6,484 (4.0%)	3,433 (17.5%)	2,555 (19.0%)	4.0%	4.0%
American Indian	713 (0.4%)	101 (0.5%)	68 (0.5%)	0.4%	0.4%
Asian/Pacific Islander	4,190 (2.6%)	318 (1.6%)	231 (1.7%)	2.6%	2.6%
Unknown	2,262 (1.4%)	86 (0.4%)	66 (0.5%)	1.4%	1.4%
Age					
50 - 59	53,559 (33.1%)	6,429 (32.8%)	4,968 (37.0%)	33.1%	33.1%
60 - 69	72,589 (44.9%)	8,716 (44.5%)	6,042 (45.0%)	44.9%	44.9%
70 - 79	35,660 (22.0%)	4,436 (22.7%)	2,429 (18.1%)	22.0%	22.0%

Table S1b. Baseline cardiovascular risk profile characteristics for WHI participants in the risk validation or treatment eligibility subcohorts

Characteristic *	WHI Risk Validation Subcohort N = 19,581	WHI Treatment Eligibility Subcohort N = 13,439	WHI N=161,808
Age, year	64 (57, 69)	63 (56, 68)	63 (57,69)
Age categories, No. (%)			
50-59	6,429 (32.8%)	4,968 (37.0%)	53,559 (33.1%)
60-69	8,716 (44.5%)	6,042 (45.0%)	72,589 (44.9%)
70-79	4,436 (22.7%)	2,429 (18.1%)	35,660 (22.0%)
Race, No. (%)			
White	8,151 (41.6%)	5,484 (40.8%)	133,541 (82.5%)
Black	7,492 (38.3%)	5,035 (37.5%)	14,618 (9.0%)
Hispanic	3,433 (17.5%)	2,555 (19.0%)	6,484 (4.0%)
American Indian	101 (0.5%)	68 (0.5%)	713 (0.4%)
Asian/Pacific Islander	318 (1.6%)	231 (1.7%)	4,190 (2.6%)
Unknown	86 (0.4%)	66 (0.5%)	2,262 (1.4%)
Clinical trial, No. (%)	14,836 (75.8%)	10,165 (75.6%)	68,132 (42.1%)
Active hormone arm	5,211 (26.6%)	3,428 (25.5%)	13,816 (8.5%)
Current smoking, No. (%)	1,748 (8.9%)	1,246 (9.3%)	11,142 (7.0%)
Diabetes, No. (%)	1,702 (8.7%)	0 (0%)	9,618 (6.0%)
Prior heart failure	0 (0%)	47 (0.4%)	1,360 (0.8%)
Prior atrial fibrillation, No. (%)	0 (0%)	378 (2.9%)	7,070 (4.4%)
Prior angina, No. (%)	774 (4.0%)	0 (0%)	8,929 (5.6%)
Prior peripheral arterial disease or arterial revascularization, No. (%)	381 (2.0%)	0 (0%)	3,635 (2.3%)
Systolic blood pressure, mm Hg	129 (118, 140)	127 (116, 139)	127 (115,138)

Antihypertensive medication, No. (%)	2,456 (12.5%)	1,303 (9.7%)	17,830 (11.0%)
Statin use at baseline, No. (%)	1,316(6.7%)	0 (0%)	12,243 (7.6%)
Aspirin use at baseline, No. (%)	3,247 (16.6%)	1,949 (14.5%)	34,001 (21.0%)
Hormone use at baseline, No. (%)	4,244 (21.7%)	3,273 (24.4%)	64,855 (40.1%)
Total cholesterol, mg/dL	226 (201, 254)	220 (198, 242)	---
HDL cholesterol, mg/dL	53 (45, 63)	54 (46, 64)	---

* Values shown are median (25^{th}, 75^{th} percentiles) or number (percentage)

Table S2. Predicted and observed risks excluding NDI events, before and after weighting to the overall WHI cohort (N=161,808)*

		Unweighted					Weighted*		
			Events in 10 years		10-year incident rate		10-year incident rate		
10-year predicted risk of ASCVD, %	N	Events / Person-years	KM-adjusted Observed	Predicted	KM-adjusted Observed (95% CI)	Predicted	KM-adjusted Observed (95% CI)	Predicted	Discrimination C-Index (95% CI)
WHI Risk Validation Subcohort									
All women	19,581	1,456 / 213,276							0.724 (0.712,0.736)
<5	6,297	128 / 71,013	107	178	0.017 (0.016,0.018)	0.028	0.013	0.027	
5 to <7.5	3,276	170 / 36,355	142	204	0.043 (0.041,0.046)	0.062	0.046	0.062	
7.5 to <10	2,626	168 / 29,002	139	228	0.053 (0.050,0.056)	0.087	0.054	0.087	
≥10	7,382	990 / 76,906	878	1,341	0.119 (0.116,0.122)	0.182	0.122	0.173	
WHI Treatment Eligibility Subcohort									
All women	13,439	753 / 148,172							0.704 (0.686,0.722)
<5	5,393	111 / 60,907	93	149	0.017 (0.016,0.019)	0.028	0.013	0.026	
5 to <7.5	2,498	128 / 27,713	106	155	0.043 (0.040,0.046)	0.062	0.047	0.062	
7.5 to <10	1,898	107 / 20,970	90	165	0.048 (0.044,0.051)	0.087	0.050	0.087	
≥10	3,650	407 / 38,582	355	554	0.097 (0.094,0.101)	0.152	0.104	0.149	

*Weighted by race/ethnicity (White, Black, Hispanic, American Indian Asian/Pacific Islander, unknown) and age (50-59, 60-69, 70-79 years)

Table S3. Unweighted and weighted predicted and observed risks before and after adjusting for statin and aspirin use during follow-up *

	N	Predicted Risk		Kaplan Meier		Statin adjusted		Aspirin adjusted		Stain & Aspirin adjusted	
		Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted
WHI risk validation cohort											
<5	6297	0.028	0.027	0.017	0.014	0.018	0.014	0.017	0.014	0.018	0.014
5 to <7.5	3276	0.062	0.062	0.044	0.047	0.045	0.048	0.044	0.047	0.046	0.049
7.5 to <10	2626	0.087	0.087	0.053	0.055	0.055	0.057	0.054	0.055	0.057	0.058
≥10	7382	0.182	0.174	0.124	0.127	0.128	0.132	0.125	0.128	0.132	0.135
Excluding active hormone arm											
<5	5042	0.028	0.027	0.018	0.014	0.018	0.014	0.018	0.014	0.018	0.015
5 to <7.5	2373	0.062	0.062	0.040	0.045	0.042	0.047	0.041	0.046	0.043	0.048
7.5 to <10	1820	0.087	0.087	0.048	0.045	0.050	0.047	0.048	0.046	0.051	0.048
≥10	5135	0.183	0.173	0.119	0.120	0.123	0.124	0.120	0.121	0.127	0.128
WHI treatment eligibility cohort											
<5	5393	0.028	0.027	0.018	0.014	0.018	0.014	0.018	0.014	0.018	0.014
5 to <7.5	2498	0.062	0.062	0.043	0.048	0.044	0.049	0.044	0.048	0.045	0.050
7.5 to <10	1898	0.087	0.087	0.048	0.050	0.050	0.052	0.049	0.051	0.051	0.053
≥10	3650	0.152	0.150	0.100	0.107	0.103	0.110	0.101	0.108	0.105	0.113
Excluding active hormone arm											
<5	4335	0.027	0.026	0.018	0.012	0.018	0.013	0.018	0.012	0.018	0.013
5 to <7.5	1814	0.062	0.062	0.037	0.043	0.039	0.045	0.038	0.044	0.040	0.046
7.5 to <10	1327	0.087	0.087	0.044	0.040	0.045	0.041	0.044	0.040	0.046	0.042
≥10	2535	0.152	0.149	0.098	0.110	0.101	0.114	0.099	0.111	0.104	0.116

*Adjustment takes into account change from baseline use of statins, aspirin, or both. Weighting takes into account the racial/ethnic and age distribution of the overall WHI cohort. Observed events are WHI-adjudicated events (including NDI events) but do not include CMS events.

Table S4a. 10-year predicted and observed risks in women 65 years and older before and after including CMS events[*]

	N	Predicted	KM-adjusted observed		Statin-adjusted[**]		Aspirin-adjusted[**]		Statin- & aspirin-adjusted[**]	
			CMS		CMS		CMS		CMS	
			-	+	-	+	-	+	-	+
I. CMS any position, PPV 85%										
WHI risk validation subcohort										
<5	197	0.043	0.033	0.044	0.034	0.044	0.034	0.044	0.034	0.045
5 to < 7.5	900	0.064	0.049	0.069	0.050	0.071	0.050	0.070	0.051	0.072
7.5 to <10	1,098	0.088	0.060	0.089	0.062	0.093	0.060	0.090	0.063	0.095
≥10	3,876	0.185	0.130	0.174	0.134	0.180	0.131	0.176	0.138	0.186
Excluding active hormone arm										
<5	126	0.043	0.027	0.037	0.027	0.037	0.027	0.038	0.027	0.038
5 to <7.5	560	0.064	0.042	0.067	0.043	0.069	0.042	0.068	0.044	0.071
7.5 to <10	655	0.087	0.046	0.078	0.048	0.081	0.046	0.079	0.049	0.083
≥10	2,574	0.187	0.126	0.176	0.131	0.183	0.128	0.178	0.135	0.189
WHI treatment eligibility subcohort										
<5	180	0.043	0.025	0.032	0.025	0.033	0.025	0.033	0.025	0.033
5 to <7.5	734	0.063	0.053	0.073	0.055	0.075	0.054	0.074	0.056	0.076
7.5 to <10	842	0.087	0.057	0.082	0.058	0.084	0.058	0.083	0.060	0.087
≥10	2,046	0.155	0.102	0.140	0.105	0.144	0.103	0.141	0.108	0.148
Excluding active hormone arm										
<5	114	0.043	0.020	0.029	0.020	0.029	0.020	0.030	0.021	0.030
5 to <7.5	460	0.064	0.044	0.068	0.046	0.070	0.045	0.069	0.047	0.072
7.5 to <10	513	0.087	0.046	0.072	0.047	0.075	0.046	0.073	0.049	0.077

≥10	1,367	0.155	0.101	0.142	0.105	0.147	0.102	0.143	0.107	0.151
II. CMS primary position only, PPV 60%										
WHI risk validation subcohort										
<5	197	0.043	0.033	0.044	0.034	0.044	0.034	0.044	0.034	0.045
5 to < 7.5	900	0.064	0.049	0.061	0.050	0.062	0.050	0.061	0.051	0.063
7.5 to <10	1,098	0.088	0.060	0.082	0.062	0.085	0.060	0.083	0.063	0.087
≥10	3,876	0.185	0.130	0.165	0.134	0.171	0.131	0.167	0.138	0.176
Excluding active hormone arm										
<5	126	0.043	0.027	0.037	0.027	0.037	0.027	0.038	0.027	0.038
5 to <7.5	560	0.064	0.042	0.053	0.043	0.055	0.042	0.054	0.044	0.056
7.5 to <10	655	0.087	0.046	0.067	0.048	0.070	0.046	0.068	0.049	0.072
≥10	2,574	0.187	0.126	0.166	0.131	0.173	0.128	0.168	0.135	0.178
WHI treatment eligibility subcohort										
<5	180	0.043	0.025	0.032	0.025	0.033	0.025	0.033	0.025	0.033
5 to <7.5	734	0.063	0.053	0.066	0.055	0.068	0.054	0.067	0.056	0.069
7.5 to <10	842	0.087	0.057	0.074	0.058	0.076	0.058	0.075	0.060	0.078
≥10	2,046	0.155	0.102	0.131	0.105	0.135	0.103	0.135	0.108	0.139
Excluding active hormone arm										
<5	114	0.043	0.020	0.029	0.020	0.029	0.020	0.030	0.021	0.030
5 to <7.5	460	0.064	0.044	0.057	0.046	0.059	0.045	0.058	0.047	0.060
7.5 to <10	513	0.087	0.046	0.062	0.047	0.064	0.046	0.063	0.049	0.066
≥10	1,367	0.155	0.101	0.133	0.105	0.138	0.102	0.134	0.107	0.141

* CMS events that were disconfirmed by WHI review of records were not included in CMS results (see supplementary methods).
**Adjustment for statin or aspirin use takes into account change from baseline use
PPV: positive predictive value

Table S4b. 10-year predicted and observed risks in women 65 years and older and enrolled in the placebo arm of the hormone therapy clinical trial (CT), after including CMS*

	N	Predicted	KM-adjusted observed	Statin-adjusted**	Aspirin-adjusted**	Statin- & aspirin-adjusted**
I. CMS any position, PPV 85%						
WHI risk validation subcohort						
<7.5	437	0.060	0.051	0.052	0.052	0.054
7.5 to <10	408	0.087	0.057	0.059	0.057	0.060
≥10	1,354	0.178	0.169	0.176	0.170	0.180
WHI treatment validation subcohort						
<7.5	362	0.059	0.047	0.048	0.047	0.050
7.5 to <10	313	0.087	0.062	0.064	0.063	0.066
≥10	719	0.151	0.140	0.145	0.141	0.148
II. CMS primary position only, PPV 60%						
WHI risk validation subcohort						
<7.5	437	0.060	0.048	0.050	0.049	0.051
7.5 to <10	408	0.087	0.057	0.059	0.057	0.060
≥10	1,354	0.178	0.160	0.166	0.161	0.171
WHI treatment validation subcohort						
<7.5	362	0.059	0.047	0.048	0.047	0.050
7.5 to <10	313	0.087	0.058	0.060	0.058	0.061
≥10	719	0.151	0.137	0.142	0.137	0.145

* CMS events that were disconfirmed by WHI review of records were not included in CMS results (see supplementary methods).
**Adjustment for statin or aspirin use takes into account change from baseline use
PPV: positive predictive value

Table S5. Treatment recommendations based on the 2013 ACC/AHA cholesterol guidelines according to racial/ethnic groups in WHI women ages 50 to 75 years old and with complete data on the risk equations

	All † N=20,473 n (%/Weighted %)	White N=8,156 n (%/Weighted %)	Black N=8,201 n (%/Weighted %)	Hispanic N=3,604 n (%/Weighted %)	Other N=512 n (%/Weighted %)	P *
Statin treatment recommended						
Clinical ASCVD**	2,383 (11.9% /9.6%)	828 (10.3%/9.1%)	1,172 (14.7%/14.9%)	341 (9.7%/9.8%)	42 (8.3%/7.5%)	<0.0001
Diabetes & LDL-C 70-189 mg/dL ††	1,684 (8.2%/6.2%)	477 (5.9%/5.5%)	922 (11.2%/11.3%)	248 (6.9%/6.9%)	37 (7.2%/7.3%)	<0.0001
LDL-C ≥190 mg/dL ††	2,622 (12.8%/12.8%)	1,118 (13.7%/13.2%)	1,090 (13.3%/13.3%)	382 (10.6%/10.6%)	32 (6.3%/6.3%)	<0.0001
10-year ASCVD risk ≥7.5% #	7,049 (34.4%/34.2%)	3,560 (43.7%/35.3%)	2,772 (33.8%/34.9%)	589 (16.3%/17.4%)	128 (25.0%/28.5%))	<0.0001
Statin treatment considered						
10-year ASCVD risk 5-<7.5% @	2,662 (13.3%/13.4%)	1,168 (14.5%/13.7%)	996 (12.5%/12.0%)	436 (12.4%/12.1%)	62 (12.2%/12.8%)	0.0005
Statin treatment not recommended						
10-year ASCVD risk <5% @	5,586 (27.8%/30.6%)	1,599 (19.8%/29.8%)	2,023 (25.3%/24.6%)	1,728 (49.1%/48.5%)	236 (46.5%/42.5%)	<0.0001

* P value from Chi-square test comparing the racial groups
**Clinical ASCVD defined as prior MI, angina, coronary revascularization, stroke, TIA, atherosclerotic peripheral arterial disease or arterial revascularization
† All = all the women with complete data on the Pooled Risk Equations and who were aged 50-75 years old; percentages are shown both unweighted and weighted to the overall WHI cohort
†† If LDL-C was missing, then we substituted non-HDL-cholesterol (=Total Chol minus HDL chol) 100-219 mg/dL
# 10-year ASCVD risk ≥7.5%, not diabetic, and LDL-C 70-189 mg/dL
@ did not meet any of the "statin treatment recommended" categories above

Supplementary Figure Legends

Figure S1 Overall study flow diagram.

Figure S2 Flow diagram for the derivation of the current analytical sample. Abbreviations: GARNET: Genomics and Randomized Trials Network; CHD: coronary heart disease; VTE: venous thromboembolism; HT: hormone therapy; WHIMS: Women's Health Initiative Memory Study; EA: estrogen arm; CT: clinical trial; OS: observational study; SHARe: SNP Health Association Resource; CVD: cardiovascular disease.

Figure S3 Statin and aspirin use at baseline and during follow-up by baseline risk category.

Figure S4 Kaplan-Meier observed WHI-adjudicated 10-year event rates before including CMS events (blue bars), WHI adjusted for aspirin/statin/CMS 10-year event rates (navy blue bars), and predicted (pink bars) 10-year risks of ASCVD events by baseline 10-year risk categories of <7.5%, 7.5 to <10%, and ≥10%, overall and by ethnic/racial groups. Abbreviations: WHI: Women's Health Initiative; CMS: Centers for Medicare and Medicaid; NDI: National Death Index; ASCVD: atherosclerotic cardiovascular disease.

Supplementary References

1. Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative study group. Controlled Clin Trials. 1998;19:61-109.
2. Hays J, Hunt JR, Hubbell FA, Anderson GL, Limacher M, Allen C, Rossouw JE. The Women's Health Initiative recruitment methods and results. Ann Epidemiol. 2003;13:S18-77.
3. Curb JD, McTiernan A, Heckbert SR, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. Ann Epidemiol. 2003;13:S122-128.
4. Lakshminarayan K, Larson JC, Virnig B, et al. Comparison of Medicare claims versus physician adjudication for identifying stroke outcomes in the Women's Health Initiative. Stroke. 2014;45:815-821.
5. Hlatky MA, Ray RM, Burwen DR, et al. Use of Medicare data to identify coronary heart disease outcomes in the Women's Health Initiative. Circ Cardiovasc Qual Outcomes. 2014;7:157-162.
6. Lemeshow S, Hosmer DW, Jr. A review of goodness of fit statistics for use in the development of logistic regression models. Am J Epidemiol. 1982;115:92-106.
7. Harrell FE, Jr., Lee KL, Mark DB. Multivariable prognostic models: Issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med. 1996;15:361-387.
8. Cook NR, Ridker PM. Response to comment on the reports of over-estimation of ASCVD risk using the 2013 AHA/ACC risk equation. Circulation. 2014;129:268-269.
9. Baigent C, Blackwell L, Collins R, et al. Aspirin in the primary and secondary prevention of vascular disease: Collaborative meta-analysis of individual participant data from randomised trials. Lancet. 2009;373:1849-1860.

Figure S1. Study flow diagram

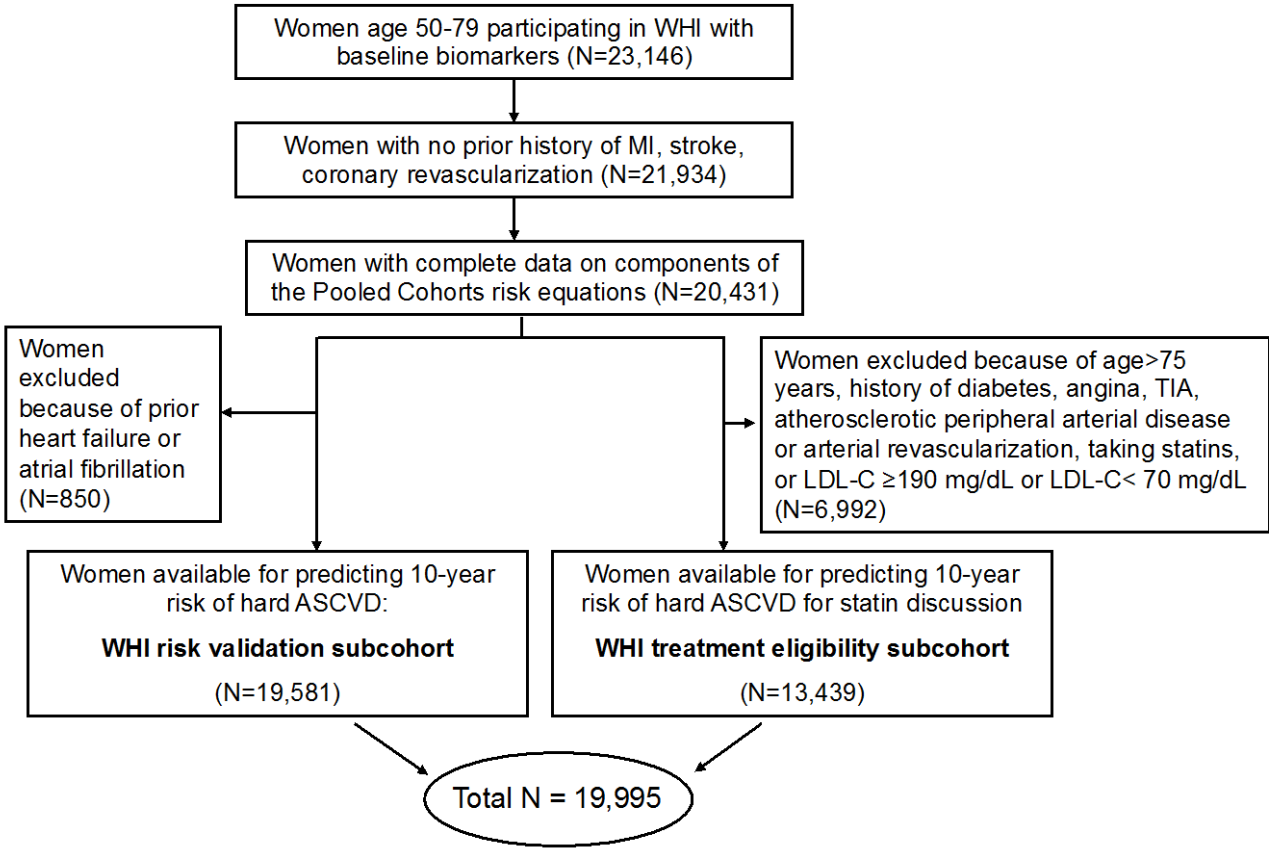


Figure S2.

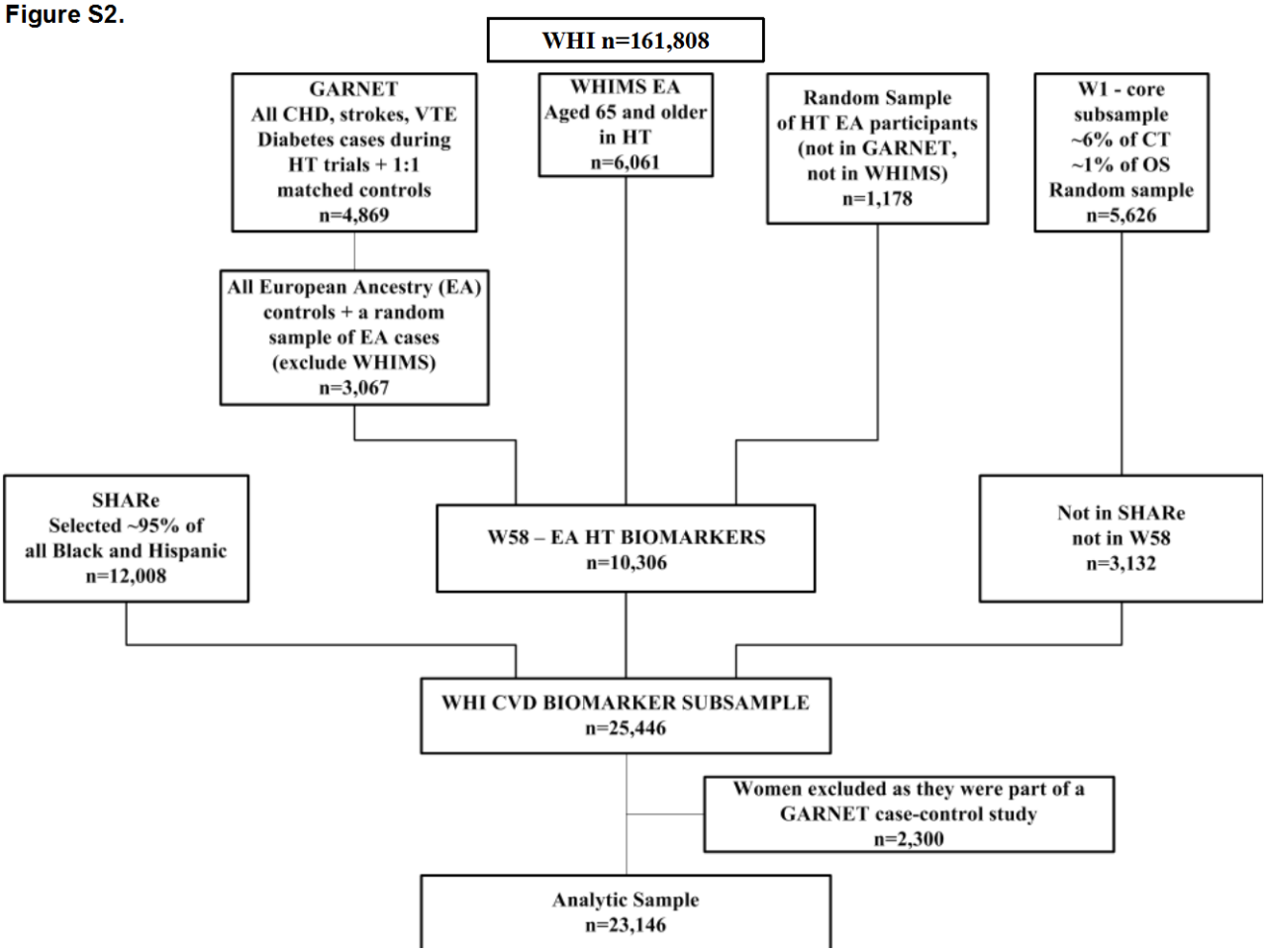


Figure S3. Statin and aspirin use at baseline and during follow-up by baseline risk category

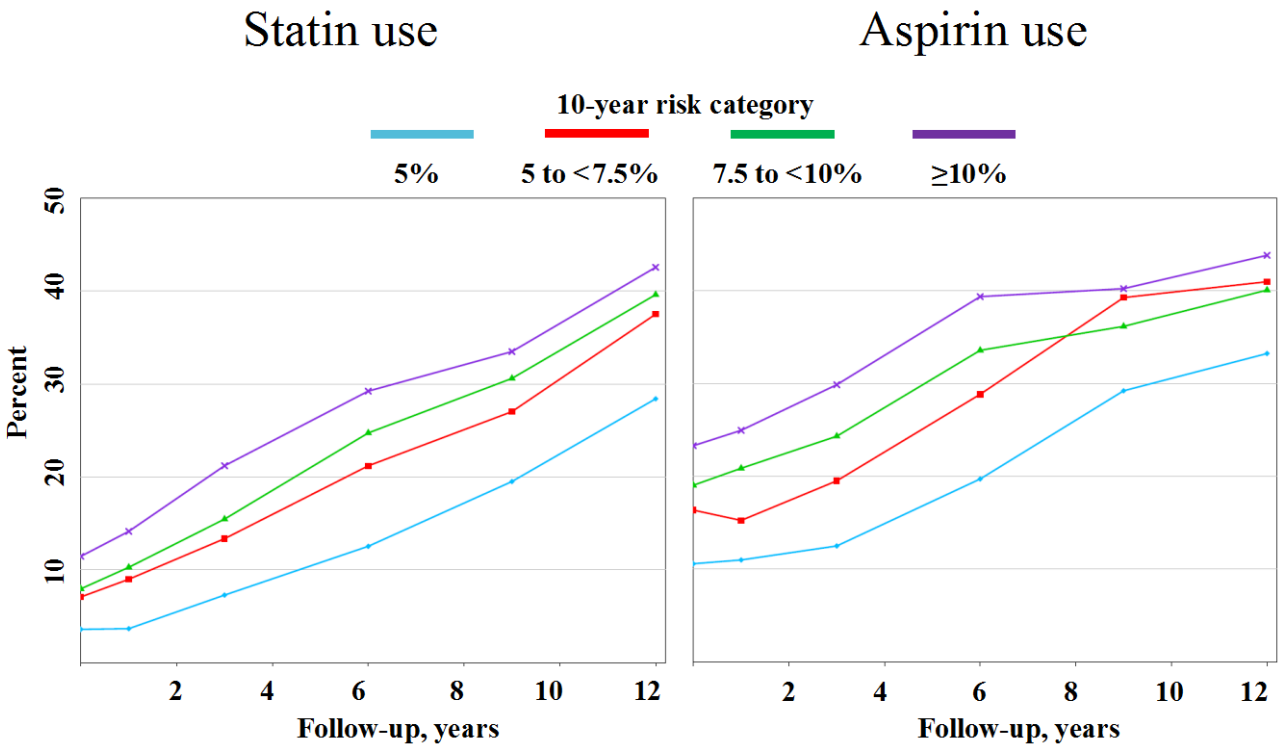
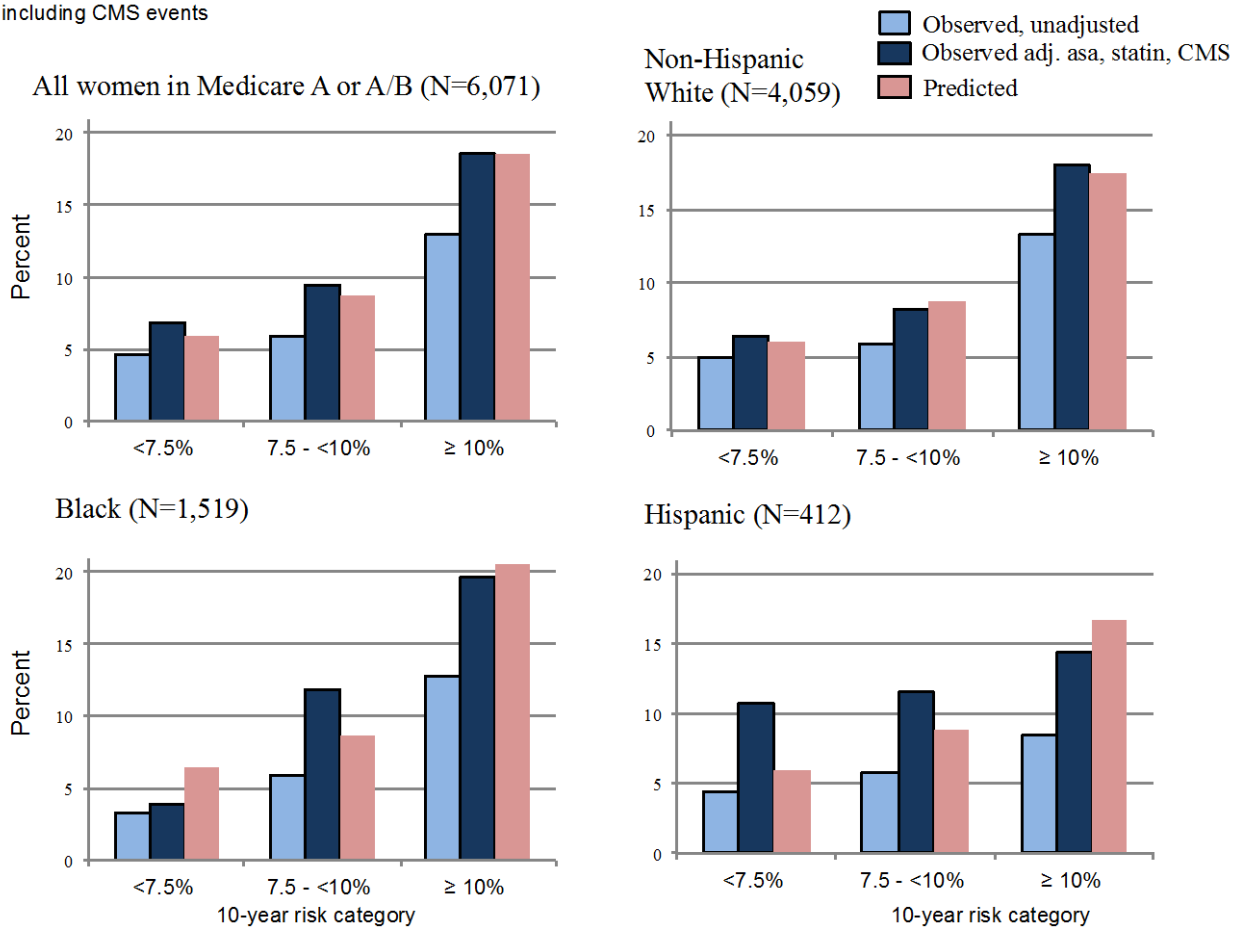


Figure S4. Observed versus predicted risk in women 65 years and older enrolled in CMS by racial/ethnic groups before and after including CMS events



SHORT LIST OF WHI INVESTIGATORS

Program Office:
(National Heart, Lung, and Blood Institute, Bethesda, Maryland)
Jacques Rossouw, Shari Ludlam, Joan McGowan, Leslie Ford, and Nancy Geller

Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA)
Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg

Investigators and Academic Centers:
(Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Arizona, Tucson/Phoenix, AZ) Cynthia A.Thomson; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher; (University of Iowa, Iowa City/Davenport, IA) Jennifer Robinson; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker; (University of Nevada, Reno, NV) Robert Brunner; (University of Minnesota, Minneapolis, MN) Karen L. Margolis Women’s Health Initiative Memory Study:(Wake Forest University School of Medicine, Winston-Salem, NC) Mark Espeland

For a list of all the investigators who have contributed to WHI science, please visit:
https://www.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Long%20List.pdf