Published in final edited form as:

J Clin Lipidol. 2010 January ; 4(1): 36–45. doi:10.1016/j.jacl.2009.12.006.

Another Treatment Gap: Restarting Secondary Prevention Medications The Women's Health Initiative

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Disclosures

Jennifer G. Robinson, MD, MPH in the past year has received:

Grants: Abbott, Bristol-Myers Squibb, Hoffman La Roche, Merck, and Merck Schering-Plough

Consultant/Advisory Board: Astra-Zeneca, Wellmark

Robert Wallace, MD

Grants/research: NIH, Pfizer

Consultant: Merck and Co.

Clinical Trial Monitoring Board: Novartis

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None.

Barbara Cochrane, PhD

None.

Mary Pettinger, MS

None.

Marcia G. Ko, MD

None.

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None.

Kamal Masaki, MD

Speaker's bureau: Pfizer

Helen Peterovich, MD

None.

Clinical Trial Identifier: NCT00000611

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Abstract

Background—Women's long-term patterns of evidence-based preventive medication utilization following a coronary heart disease (CHD) diagnosis have not been sufficiently studied.

Methods—Postmenopausal women 50–79 years were eligible for randomization in the Women's Health Initiative's (WHI) hormone trials if they met inclusion and exclusion criteria and were >80% adherent during a placebo-lead-in period and in the dietary modification trial if they were willing to follow a 20% fat diet. Those with adjudicated myocardial infarction or coronary revascularization after the baseline visit were included in the analysis (n=2627). Baseline visits occurred between 1993 and 1998, then annually until the trials ended in 2002 through 2005; medication inventories were obtained at baseline and years 1, 3, 6 and 9.

Results—Utilization at the first WHI visit following a CHD diagnosis increased over time for statins (49% to 72%; $p<0.0001$), beta-blockers (49% to 62%; $p=0.003$), and angiotensin-converting enzyme inhibitors/angiotensin-II receptor blockers (ACEI/ARBs) [26 to 43%; $p<0.0001$]. Aspirin use remained stable at 76% ($p=0.09$). Once women reported using a statin, aspirin, or beta-blocker, 84–89% reported use at 1 or more subsequent visits, with slightly lower rates for ACEI/ARBs (76%). Statin, aspirin, beta-blocker, or ACEI/ARB use was reported at 2 or more consecutive visits by 57%, 66%, 48%, and 28% respectively. These drugs were initiated or resumed at a later visit by 24%, 17%, 15%, and 17%, respectively, and were never used during the period of follow-up by 19%, 10%, 33%, and 49% respectively.

Conclusions—Efforts to improve secondary prevention medication utilization should target both drug initiation and restarting drugs in patients who have discontinued them.

Keywords

Secondary prevention; Adherence; Statins; Women; Coronary heart disease

Extensive clinical trial evidence demonstrates that statins, aspirin, beta-blockers, angiotensin-converting enzyme inhibitors (ACE) and angiotensin-II receptor blockers (ARB) in patients with coronary heart disease (CHD) can substantially reduce the risk of heart attack, stroke, and all-cause mortality by 16% to 63%.¹ Declining cardiovascular mortality in the elderly is largely attributed to these evidence-based therapies.² Current guidelines recommend statins and low-dose aspirin for the vast majority of patients with CHD as well as other vascular disease.³ Beta-blockers are indicated following MI and acute coronary syndromes. For hypertensive CHD patients, blood pressure control with beta-blockers, ACE inhibitors, and other drugs such as thiazides is recommended. ACE-inhibitors are further recommended for those with impaired left ventricular function, diabetes, or chronic kidney disease.

The long-term survival advantages associated with improved statin and beta-blocker adherence after acute myocardial infarction appear to be mediated by drug effects rather than an epiphenomenon of "healthy adherer" behavioral attributes.⁴ Although substantial progress has

been made over the past four decades,⁵ significant treatment gaps still exist in the use of secondary prevention medications. The highest risk patients, those with coronary heart disease (CHD) over age 65, experience the largest treatment gaps.⁶ Since drug utilization rates decline significantly over time, long term control of multiple risk factors is rare.⁷

Some data suggest women with CHD have lower rates of secondary prevention medication use than men.⁸ We therefore evaluated the large cohort of women with CHD participating in the Women's Health Initiative (WHI) Clinical Trials in order to describe trends in long-term utilization of secondary prevention medications. These studies provided a unique opportunity to describe drug utilization patterns over 9 years in older women selected for adherence before enrollment in the WHI hormone and/or dietary modification trials. Women were randomized in the hormone trials if, after meeting eligibility criteria, they were >80% adherent by pill count during a 28-day placebo lead-in period.⁹ Women were randomized in the dietary modification trial if they met eligibility criteria and were willing to change their eating patterns by greatly reducing dietary fat intake and increasing fruit/vegetable and grain intake.¹⁰

Methods

Study population

This was a *post hoc* analysis of data collected for the WHI clinical trials. Details of the study design, eligibility criteria, recruitment methods, methodology, and baseline characteristics have been previously published for the WHI's hormone and Dietary Modification clinical trials.^{9–11} Briefly, between 1993 and 1998, 40 clinical centers throughout the United States recruited a multiethnic population of postmenopausal women aged 50 to 79 years for participation in trials of postmenopausal hormone therapy, dietary modification, and calcium and vitamin D supplementation. Participants were recruited primarily through mass mailings to age-eligible women. Major exclusions for the hormone trials included conditions related to safety, competing risk, and adherence and retention concerns. Eligible women (n=10,739) who had undergone a hysterectomy were randomly assigned to receive 0.625 mg/d of oral conjugated equine estrogen (CEE) [Premarin; Wyeth, St. Davids, Pa] or a matching placebo (E-Alone trial).¹² Eligible women (n=16,608) with an intact uterus were randomized to receive 0.625 mg of oral CEE and 2.5 mg of medroxyprogesterone acetate (MPA) [Prempro; Wyeth, St. Davids, Pa] or 0.625 mg of CEE alone or a matching placebo (E+P trial). The Diet Modification trial randomized 48,835 women to a low-fat eating pattern (40%) or a self-selected dietary behavior (60%).¹⁰ Major exclusions from the dietary modification trial were a diet <32% fat, incompatible medical conditions, frequent restaurant dining, and a history of breast or colon cancer. A total of 8,050 women participated in both the diet and hormone trials. The protocol and consent forms were approved by the institutional review boards for all participating institutions. We analyzed baseline and annual visits 1, 3, 6, and 9 as of the termination dates for the Hormone Trials (July, 2002 for the E+P trial; February 29, 2004 for the E-alone trial; and March, 2005 for the Diet Modification trial). Baseline and annual visits occurred in overlapping time intervals (baseline: 9/14/1993 to 8/4/1998; visit 1: 11/1/1994 to 11/22/2000; visit 3: 11/11/1996 to 2/21/2003; visit 6: 11/1/1999 to 2/1/5/2005; and visit 9: 11/14/2002 to 11/8/2004). Women in the E+P trial were followed for an average of 5.2 years, those in the E-alone trial for 6.8 years, and the Diet Modification for 8.1 years.^{12–14}

Women without self-reported CHD at baseline who experienced an adjudicated CHD event prior to their last WHI visit were included in the main analysis. CHD events were defined as the first of either a myocardial infarction or coronary revascularization (percutaneous transluminal coronary angioplasty/stent or coronary artery bypass surgery). Methods for CHD event ascertainment have been described elsewhere.¹⁴ In brief, medical records including electrocardiograms, cardiac enzymes, procedure reports and discharge summaries from women reporting an overnight hospitalization were reviewed by local or central adjudicators. The first

myocardial infarction or revascularization outcome was centrally adjudicated by trained physicians using standard diagnostic criteria in the hormone trials; non-hormone trial Diet Modification events were locally adjudicated.¹⁵ Additional analyses in all first MIs and in all first revascularizations evaluated medication utilization.

An additional analysis evaluated medication utilization patterns in women reporting incident CHD to their last WHI visit. Self-reported CHD was defined as a “yes” answer to one of the questions, “Has your doctor ever told you that you had heart problems?”; If yes, “Please mark the conditions or procedures below that your doctor said you had: cardiac arrest (where your heart stopped and needed to be restarted)/heart failure or congestive heart failure/cardiac catheterization/heart bypass operation or coronary bypass surgery for blocked or clogged arteries in your heart/angioplasty of the coronary arteries (opening of the arteries of the heart with a balloon or other device, sometimes called a PTCA)”; “Did your doctor ever say that you had a heart attack? This is sometimes called a coronary, myocardial infarction, or MI.”; or “Did your doctor ever say you had angina (chest pains from a heart problem)?”. Self-report of CHD was considered to be the more appropriate measure of a woman’s perception of her health status and need for medications.

Women were asked to bring all current prescription and nonprescription medications in their original containers to the baseline and year 1, 3, 6, and 9 clinic visits. Trained personnel entered the product or generic name of the medications on the label into the study database and then matched it to the corresponding item in a pharmacy database [Master Drug Data Base: Medi-Span, Indianapolis, IN]. The 7 classes of cardiovascular medications evaluated in this analysis were aspirin, statins, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARB), calcium channel blockers, and other antihypertensive agents (including thiazide-type diuretics, antiadrenergic agents, and thiazide-combinations and other antihypertensive combinations). Aspirin use was defined as ≥ 80 mg per day for at least 30 days. Visits subsequent to the first CHD event were evaluated for medication use. Use at 2 consecutive visits was evaluated only in those attending 2 or more visits after the first CHD event.

Statistical analysis

The purpose of this paper is primarily descriptive. Baseline characteristics were compared across the three mutually exclusive WHI trial groups using chi-square tests and F-tests for differences within the category. Trends in medication use over the follow-up period are displayed graphically using only the first visit after the CHD diagnosis. Frequency of each type of medication use was determined at all available visits after the CHD self-report. Frequencies were computed as the number of women with CHD reporting medication use, divided by the total number of women with CHD at a given visit. Statistical comparisons were made within a drug class, but not between drug classes since many participants were taking more than one drug. Similarly no statistical comparisons were made between those with myocardial infarctions and those with revascularizations, since 33% had both. Ninety-five percent confidence intervals for each reported percentage were based on a binomial distribution. P-values < 0.05 were considered significant. SAS version 9.1 was used for the analysis.¹⁶

Results

Baseline characteristics of the 2627 participants with incident CHD in each of the 3 clinical trials are presented in Table 1. More than half of the women with incident CHD were enrolled only in the Diet Modification trial. The greatest proportion of minority women were in the E-alone trial. Other baseline demographic characteristics were modestly different among the 3 studies. Risk factor levels differed significantly among the 3 trials, with women in the E-alone trial having the highest frequency of risk factors and women in the E+P trial having the lowest

risk factor burden. Women in the Diet Modification trial had the highest rates of insurance, doctor visits in the past year, income level, and number of total medications. The rates of medication utilization at each visit, persistence of use, and discontinuation were very similar for women in the hormone and the diet modification trials (data not shown), supporting the combination of the 3 trials for the analysis.

Trends in the prevalence of statin, aspirin, and beta-blocker use at the first visit after CHD diagnosis from 1994 to 2004 are presented in Figure 1. Statin use increased from 49% (95% CI 42–57%) to 72% (95% CI 68–76%) over the period of follow-up (47% increase; p for trend <0.0001), aspirin use stayed stable at 76% (95% CIs 70–82% and 72–80%; $p=0.09$), and beta-blocker use increased from 49% (95% CI 42–57%) to 62% (95% CI 58–67%) [27% increase; p for trend $=0.003$]. The concomitant use of a statin and aspirin increased from 41% (95% CI 34–49%) to 58% (54–63%) [41% increase; p for trend <0.0001]. Trends in the use of ACE inhibitors, ARBs, calcium blockers, and other antihypertensives are presented in Figure 2. ACE inhibitor use did not significantly increase [21 (95% CI 16–28%) to 27% (95% CI 23–31%); p for trend 0.39], ARB use increased from 5% (95% CI 3–10%) to 16% (95% CI 12–19%) (220% increase; p for trend <0.0001), and the use of either an ACE or ARB increased from 25% (95% CI 20–38%) to 42% (95% CI 37–47%) [68% increase; p for trend <0.0001]. The use of other antihypertensives increased from 14% (95% CI 10–20%) to 31% (95% CI 30–36%) (121% increase; p for trend <0.0001). Calcium channel blocker use remained stable over time, 30% (95% CI 24–37%) and 23% (95% CI 19–27%) [p for trend 0.35].

Table 2 shows the proportion of women at each visit who were taking or not taking a medication. For the 2nd and 3rd visit following CHD diagnosis, the proportion of women attending the visit is displayed to reflect use of the drug at the previous visit and drug use at that visit. Of those on a statin, aspirin, or beta-blocker at the first visit after CHD diagnosis, use was reported in 88%, 84%, and 86%, respectively, at the next visit 2–3 years later (Table 2). Although relatively few of these women had a third visit after CHD diagnosis, 90%, 84%, and 88% were still using a statin, aspirin, or beta-blocker, respectively, at the third visit. Use of an ACE inhibitors or ARB at both the first and second visits was slightly lower at 75–76%.

In the 38% women not on a statin after the first visit following CHD diagnosis, 40–45% were taking a statin at the next visit, and 84% continued use at the third visit (Table 2). Of the 26% of participants not on aspirin after the first visit following CHD diagnosis, 43–53% were taking aspirin by the next visit, and 88% continued use at a third visit. In the 42% of women who were not on a beta-blocker after the first visit following CHD diagnosis, 18–25% were taking a beta-blocker by the next visit, and 72% continued use at a third visit. In the 60% of women who were not on an ACE inhibitors or ARBs after the first visit following CHD diagnosis, 19–22% were on a drug in this class by the next visit and 65% continued use at a third visit.

Only 60% of women with incident CHD were using a statin at 2 or more visits, with a slightly higher rate for aspirin (66%) and a slightly lower rate (48%) for beta-blockers (Table 3); 12% were using none of the 4 drug classes, 20% used just one drug class, 33% were using 2 drug classes, 27% were using 3 drug classes, and 8% were taking all 4 drug classes. Of women not on a statin at the first visit following CHD diagnosis, or who had discontinued the statin by the 2nd visit, only 23% initiated or resumed a statin at a subsequent visit. Similar low rates of initiation or resumption at a subsequent visit occurred for aspirin (17%), beta-blockers (15%) and ACE inhibitor/ARBs (17%). Looked at in another way, of women with incident CHD, fewer women reported never using a statin (20%) or aspirin (10%) than a beta-blocker (33%) or an ACE inhibitor or ARB (49%).

Use of statins, aspirin, beta-blockers, and ACE/ARBs at each visit was almost identical in those with myocardial infarction as the first CHD event ($n=1369$) as in those with revascularization

as the first CHD event (n=2118) [data not shown]. Use at 2 or more consecutive visits, respectively for myocardial infarction and revascularization first events, was 54% and 61% for statins, 65% and 67% for aspirin, 49% for both for beta-blockers, and 30% and 29% for ACE/ARBs. Later initiation or resumption, and never use, were also similar for the 2 types of first events.

Women with self-reported incident CHD (n=4537), were less likely to report use of a secondary prevention medication at the first visit following CHD diagnosis [45% (95% CI 44–47%) for statin, 60% (95% CI 58–61%) for aspirin, 45% (95% CI 43–47%) for beta-blockers, and 34% (95% CI 32–36) for ACE/ARB. However, rates of persistent use (85–89% for statins, 80–81% for aspirin, 86–88% for beta-blockers, and 75–79% for ACE/ARBs) were similar to women with adjudicated CHD.

Discussion

Statins, aspirin, beta-blockers, ACE inhibitors, and ARBs use at the first WHI visit after CHD diagnosis increased markedly between 1993 and 2004. In this analysis of women who were pre-selected for adherence as a requirement for clinical trial participation, use at the first visit following CHD diagnosis had a major impact on long-term utilization. If a woman reported use at the first visit following CHD diagnosis, about 85% remained on a statin, aspirin, or a beta-blocker at a subsequent visits, and about 75% remained on an ACE/ARB. The second striking finding was the low rate of starting a medication after the first visit following CHD diagnosis, or restarting a medication class once it was discontinued—only 24% of those not previously on a statin started one during the period of follow-up, and about 16% for the other major prevention medication drug classes. Both findings underscore the importance that physician prescribing practices can play in maintaining long-term utilization of secondary prevention medication.

The rates of statin and aspirin use in our analysis of women with chronic CHD were higher than those reported at 30 days post-MI for large Medicare database during the same period. In this analysis of over 21,000 post-MI Medicare patients, 73% were women and the mean age was 80 years.² By 2004, use of statins had increased to 51% (versus 72% in our analysis) and antiplatelet agents to 51% (versus 76% in our analysis). As would be expected in a purely post-MI population, the rate of beta-blocker use was higher at 72% (versus 62% in our analysis) as was ACE inhibitor/ARBs use 50% (versus 43% in our analysis). In a database of almost 100,000 patients from hospitals participating in the Get With The Guidelines-CAD hospital performance improvement program between 2000 and 2005, men were more 25% more likely to receive a statin at discharge than women.⁸ However, another analysis confined to Medicare patients aged ≥ 65 years, found no evidence of a gender difference in post MI use of statins, beta-blockers, and ACE inhibitors or ARBs.¹⁷

Suboptimal rates of secondary prevention medication use in WHI participants may include disparities in medication prescription at hospital discharge^{18–20} or medication discontinuation prior to the first WHI visit following CHD diagnosis, both of which have been reported to occur disproportionately in women with advancing age.⁷ Most drug discontinuations appear to occur within one month of hospital discharge with rates relatively stable over the remaining 1 year.⁷ These data further supports systematic efforts to increase rates of medication prescription at discharge, such as the American Heart Association's Get With The Guidelines program. Our data suggest these efforts may result in higher rates of medication utilization long-term.

Continuous use of secondary prevention medications was disappointingly low in this cohort of health conscious older women thought generally to be adherent. Rates of continuous use at

2 consecutive visits of a statin (57%), aspirin (66%), or beta-blocker (48%) were suboptimal. Some women did, however, initiate or restart a drug at a later visit. This finding is consistent with an analysis of a Canadian insurance database in which 53% of new statin users had a period of nonadherence of at least 90 days, with 48% restarting treatment within 1 year and 60% by 2 years.²¹ Adverse hepatic or muscle events were reported in <1% of patients who discontinued statin therapy in the Canadian database. A 6-fold increase in restarting a statin was associated with visits to the physician who initiated statin treatment, a 3-fold increase was associated with visits to another physician, a 3.6-fold increase was associated with a cardiovascular disease hospitalization, and a 1.5-fold increase was associated with a cholesterol test. Other studies have found higher rates of statin and beta-blocker discontinuation over time. These studies were comprised predominantly of men, without data presented separately for women. The Duke Databank for Cardiovascular Disease (≥ 1 cardiac procedure with at least 2 follow-up surveys returned between 1995 and 2002; 70% male; and without CHF) found at the first follow-up survey in 2002 that the rate of aspirin use was 83%, lipid-lowering agents was 63%, beta-blockers was 61%, and all 3 drugs was 39%.²² Consistent use of aspirin over the next 2 annual surveys was reduced to 71%, beta-blockers to 46%, and lipid-lowering agents to 43%, while 21% reported consistent use of all 3 medications. Taken together, these findings suggest that interventions to improve continuous drug use by patients need to be accompanied by interventions to encourage physicians and patients to initiate or restart a secondary prevention medications after discontinuation. Routine cholesterol testing in patients with CHD along with routine medication inventories may be strategies for increasing continuous medication use.

Rates of ACE inhibitor and ARB use were lower than that of aspirin, statins, and beta-blockers, as might be expected given the more limited indications for use during this time period for hypertension, post-myocardial infarction patients with impaired left ventricular dysfunction or diabetic patients.^{23,24}

Limitations of this study include that the WHI clinical trials were not a population-based sample. Women participating in the WHI clinical trials had several characteristics that may have enhanced long-term secondary prevention drug use. Not only were they more health conscious than average, they were also willing to regularly take hormone pills or adhere to a low fat diet in a long-term clinical trial. Nevertheless, one might expect that this greater health consciousness might have selected a sample of “ideal patients” in whom prescribing patterns might be expected to be better than average. As such, our findings are a cause for even greater concern. As discussed above, rates of persistence of drug use may differ in more typical populations, where factors such as competing demands for economic resources could play a bigger role.^{22,26}

Although we cannot definitively separate lack of prescribing from patient adherence, our findings are highly suggestive that prescribing plays an important role, since once a women reported using a medication, she had at least an 80% probability of being on a drug in that class at the each subsequent visit. Support for this hypothesis also comes from the analysis of self-reported CHD. Although utilization of secondary prevention medications at the first visit following self-report of CHD was lower than for adjudicated CHD, utilization at subsequent visits was still about 80% or more. It should also be noted that the method of CHD documentation should therefore be considered when comparing studies of medication utilization.

By selecting a population of generally adherent individuals, we were able to provide additional support that physician prescribing behavior plays a major role not just in starting a secondary prevention medication but in continued long-term use. Future efforts to modify physician prescribing patterns should focus on re-prescribing discontinued drugs at later visits, in addition

to initiating therapy following a CHD event. Effective interventions to enhance patient adherence are necessary as well. Such strategies are likely to have a substantial impact on long-term survival of women with CHD.

Conclusion

Healthcare providers should take the opportunity at every follow-up visit to encourage patients to continue secondary prevention medications, and to restart discontinued secondary prevention medications.

Acknowledgments

This project was also supported (or supported in part) by an Agency for Healthcare Research and Quality (AHRQ) Centers for Education and Research on Therapeutics cooperative agreement #5 U18 HSO16094.

List of abbreviations

ACE/ARB	angiotensin-converting enzyme inhibitors/angiotensin-II receptor blockers
CEE	conjugated equine estrogen
CHD	coronary heart disease
CI	confidence interval
MI	myocardial infarction
MPA	medroxyprogesterone acetate
WHI	Women's Health Initiative's

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Appendix

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Figure 1. Aspirin, statin, and beta-blocker utilization at first visit following an adjudicated CHD diagnosis

Figure 2. ACE-inhibitor, ARB, calcium channel blocker and other antihypertensive use at first visit following an adjudicated CHD diagnosis

Baseline characteristics of older women with adjudicated CHD during participation in the Women's Health Initiative Hormone and Diet Modification Trials

Table 1

	All N=2627 N (%)	E+P N=659 (25%) N (%)	E-Alone N=528 (20%) N (%)	Diet only N=1440 (55%) N (%)	p-value
Age					
50–59	494 (19)	128 (19)	90 (17)	276 (19)	0.60
60–69	1283 (49)	317 (48)	254 (48)	712 (49)	
70–79	850 (32)	214 (32)	184 (35)	452 (31)	
Region					
Midwest	621 (24)	181 (27)	140 (27)	300 (21)	<0.0001
Northeast	652 (25)	156 (24)	110 (21)	386 (27)	
South	710 (27)	171 (26)	168 (32)	371 (26)	
West	644 (25)	151 (23)	110 (21)	383 (27)	
Race/ethnicity					
American Indian	10 (0.4)	1 (0.1)	3 (1)	6 (0.4)	<0.0001
Asian/Pacific Islander	33 (1)	10 (2)	5 (1)	18 (1)	
Black	228 (9)	40 (6)	58 (11)	130 (9)	
Hispanic	71 (3)	26 (4)	24 (5)	21 (1)	
White	2248 (86)	568 (86)	431 (82)	1249 (87)	
Unknown	37 (1)	14 (2)	7 (1)	16 (1)	
Stroke	59 (2)	12 (2)	18 (3)	29 (2)	0.13
Peripheral arterial disease	75 (3)	17 (3)	17 (3)	41 (3)	0.80
Diabetes	439 (17)	110 (17)	114 (22)	215 (15)	0.002
Hypertension	957 (42)	206 (35)	190 (41)	561 (45)	0.002
Yes - untreated	221 (10)	68 (12)	50 (11)	103 (8)	
Smoking					
Current	304 (12)	96 (15)	88 (17)	120 (8)	<0.0001
Never	1240 (48)	290 (45)	262 (50)	688 (48)	
Past	1047 (40)	261 (40)	172 (33)	614 (43)	
BMI					
<25	552 (21)	164 (25)	102 (19)	286 (20)	0.08
25–<30	951 (36)	234 (36)	192 (36)	525 (37)	
≥30	1120 (43)	261 (40)	234 (44)	625 (44)	
Insurance coverage	2481 (95)	611 (93)	479 (93)	1391 (97)	<0.0001
Doctor visit in past year	2106 (83)	509 (79)	396 (79)	1201 (86)	<0.0001

	All N=2627 N (%)	E+P N=659 (25%) N (%)	E-Alone N=528 (20%) N (%)	Diet only N=1440 (55%) N (%)	p-value
Income					
<\$10,000	144 (6)	27 (4)	55 (11)	62 (6)	<0.0001
\$10,000–<20,000	528 (21)	149 (24)	146 (29)	233 (17)	
\$20,000–<35,000	728 (29)	197 (32)	134 (26)	397 (29)	
\$35,000–<50,000	500 (20)	112 (18)	82 (16)	306 (22)	
\$50,000–<75,000	376 (15)	86 (14)	69 (14)	221 (16)	
≥\$75,000	213 (9)	50 (8)	20 (4)	143 (11)	
Number of medications					
0	341 (13)	124 (19)	75 (14)	142 (10)	<0.0001
1	419 (16)	122 (19)	93 (18)	204 (14)	
2	470 (18)	127 (19)	103 (20)	240 (17)	
3	378 (14)	91 (14)	70 (13)	217 (15)	
4	355 (14)	82 (12)	68 (13)	205 (14)	
5	230 (9)	42 (6)	43 (8)	145 (10)	
6–7	261 (10)	43 (7)	48 (9)	170 (12)	
≥8	173 (7)	28 (4)	28 (5)	117 (8)	

E+P = Estrogen plus Progestin trial

E-Alone = Estrogen only trial

Table 2

Proportion of women at each visit who were taking or not taking a secondary prevention medication following an adjudicated CHD diagnosis. For the 2nd and 3rd visit after the first visit following a CHD diagnosis, the proportion of women attending the visit is displayed to reflect use of the drug at the previous visit and drug use at that visit.

Drug class	On drug at 1 st visit after Diagnosis	n/N* Percent (95% CI) attending 1 st visit	On drug at 2 nd visit after diagnosis	n/N* Percent (95% CI) attending 2 nd visit	On drug at 3 rd visit after diagnosis	n/N* Percent (95% CI) attending 3 rd visit
Statins	Yes	1039/1669 62.3 (59.9, 64.6)	Yes	371/423 87.7 (84.2, 90.7)	Yes	86/96 89.6 (81.7, 94.9)
					No	10/96 10.4 (5.1, 18.3)
			No	52/423 12.3 (9.3, 15.8)	Yes	10/15 66.7 (38.4, 88.2)
Statins	No	630/1669 37.8 (35.4, 40.1)	Yes	134/298 45.0 (39.2, 50.8)	No	5/15 33.3 (11.8, 61.6)
					Yes	43/51 84.3 (71.4, 93.0)
			No		No	8/51 15.7 (7.0, 28.6)
			No	164/298 55.0 (49.2, 60.8)	Yes	26/65 40.0 (28.0, 52.9)
					No	39/65 60.0 (47.1, 72.0)
			Yes	456/542 84.1 (80.8, 87.1)	Yes	123/147 83.7 (76.7, 89.3)
Aspirin	Yes	1240/1669 74.3 (72.1, 76.4)	Yes		No	24/147 16.3 (10.8, 23.3)
			No	86/542 15.9 (12.9, 19.2)	Yes	16/25 64.0 (42.5, 82.0)
					No	9/25 36.0 (18.0, 57.5)
Aspirin	No	4297/1669 25.7 (23.6, 27.9)	Yes	94/179 52.5 (44.9, 60.0)	Yes	22/25 88.0 (68.8, 97.5)
					No	3/25 12.0 (2.6, 31.2)
			No	85/179 47.5 (40.0, 55.1)	Yes	13/30 43.3 (25.5, 62.6)

Drug class	On drug at 1 st visit after Diagnosis	n/N* Percent (95% CI) attending 1 st visit	On drug at 2 nd visit after diagnosis	n/N* Percent (95% CI) attending 2 nd visit	On drug at 3 rd visit after diagnosis	n/N* Percent (95% CI) Attending 3 rd visit
Beta-blocker	Yes	965/1669 57.8 (55.4, 60.2)	Yes	330/385 85.7 (81.8, 89.1)	Yes	88/100 88.0 (80.0, 93.6)
			No	55/385 14.3 (11.0, 18.2)	No	12/100 12.0 (6.4, 20.0)
					Yes	5/15 33.3 (11.8, 61.6)
					No	10/15 66.7 (38.4, 88.2)
Beta-blocker	No	704/1669 42.2 (39.8, 44.6)	Yes	84/336 25.0 (20.5, 30.0)	Yes	13/18 72.2 (46.5, 90.3)
					No	5/18 27.8 (9.7, 53.5)
			No	252/336 75.0 (70.0, 79.5)	Yes	17/94 18.1 (10.9, 27.4)
					No	77/94 81.9 (72.6, 89.1)
ACEI/ARB	Yes	667/1669 40.0 (37.6, 42.4)	Yes	186/245 75.9 (70.1, 81.1)	Yes	39/52 75.0 (61.1, 86.0)
					No	13/52 25.0 (14.0, 39.0)
			No	59/245 24.1 (18.9, 29.9)	Yes	2/9 22.2 (2.8, 60.0)
					No	7/9 77.8 (40.0, 97.2)
ACEI/ARB	No	1002/1669 60.0 (57.6, 62.4)	Yes	90/476 18.9 (15.5, 22.7)	Yes	17/26 65.4 (44.3, 82.8)
					No	9/26 34.6 (17.2, 55.7)
			No	386/476 81.1 (77.3, 84.5)	Yes	29/140 20.7 (14.3, 28.4)
					No	111/140 79.3 (71.6, 85.7)

ACEI/ARB=Angiotensin converting enzyme inhibitor/angiotensin-II receptor blocker

* n/N = number meeting criteria/number attending that visit

Table 3

Continued use, later initiation or resumption of use, and never use of secondary prevention medications following adjudicated CHD diagnosis (mean percent with 95% confidence intervals)

Drug class	% on med at 2 or more consecutive visits *	% initiating drug at 2nd or 3rd visit after CHD diagnosis or resumed med use after discontinuation	% who did not receive med at any visit following CHD diagnosis
Statin	57.3 (53.7, 61.0)	23.7 (20.7, 27.0)	19.1 (16.3, 22.1)
Aspirin	65.6 (62.0, 69.0)	16.9 (14.2, 19.8)	10.3 (8.2, 12.7)
Beta-blocker	47.6 (43.9, 51.3)	14.7 (12.2, 17.5)	32.9 (29.5, 36.5)
ACE I/ARB	28.4 (25.2, 31.8)	17.0 (14.4, 19.9)	49.4 (45.7, 53.1)

ACEI/ARB=Angiotensin converting enzyme inhibitor/angiotensin-II receptor blocker

* Of women with 2 or more visits following CHD diagnosis