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## Aspirin as Primary Prevention of Acute Coronary Heart Disease Events

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## Abstract

**Background/Objective**—Aspirin for primary prophylaxis is controversial. This study evaluated associations between prophylactic aspirin use and incident acute coronary heart disease (CHD) events.

**Methods and Results**—The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study was accessed for aspirin use examining black and white hazards for incident CHD, for men and women, each adjusting incrementally for sampling, sociodemographics, and CHD risk factors. Stratified models examined risks across strata of the Framingham risk score, and all-cause mortality. 23,949 participants (mean 64 yo), had 503 incident events over a 3.5 year follow-up. Prophylactic aspirin use was not associated with incident acute CHD, HR 1.05 (95% CI 0.86, 1.29). Modeling had little impact on the HR (1.09 {95% CI 0.89, 1.33) nor did the addition of risk factors (HR 1.00 {95% CI 0.81, 1.23). Aspirin use was not associated with incident CHD for any Framingham risk level. Findings were similar when including all aspirin users (not just those taking aspirin prophylactically), and when examining associations with all-cause mortality. There was no excess hospitalized bleeding in the aspirin users.

#### Authors' contributions

#### CONSENT

Consent for examinations and anonymous publication of findings was obtained verbally by telephone and subsequently in writing during a follow-up in-home visit.

#### ETHICAL APPROVAL

#### **COMPETING INTERESTS**

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This work was carried out in collaboration between all authors. Author SPG designed the ancillary study, wrote the protocol, and wrote the first draft of the manuscript. Authors MH and GH performed the statistical analysis. Authors TMB, GH, MH and MMS managed the analyses of the study and contributed to the drafting of the manuscript. All authors read and approved the final manuscript.

All authors hereby declare that all proposed analyses have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

There are no conflicts to report for any of the authors, except Dr. Howard who is on the Executive Committee for the Aspirin to Reduce Risk of Initial Vascular Events (ARRIVE) Study, sponsored by Bayer.

**Conclusion**—Aspirin was not associated with lower risk for incident acute CHD overall, or within race, gender, or Framingham Risk Score.

#### Keywords

Aspirin; prophylaxis; incident; coronary; heart; disease

## **1. INTRODUCTION**

Aspirin is an effective anti-platelet and anti-inflammatory agent [1]. In a meta-analysis of trials of aspirin in the secondary prevention of cardiovascular and cerebrovascular events, aspirin significantly reduced the number of strokes and myocardial infarctions (MI) [2]. The data for long-term primary prevention are less clear. Nevertheless, aspirin is currently recommended as primary prevention for some men and women, particularly those over age 65 [3]. The use of aspirin for primary prevention is still undergoing study in at least 1 ongoing intervention trial [4]. It has been suggested that lower dose aspirin might mitigate some of the bleeding complications attendant with aspirin use, but, the effectiveness of a lower dose remains uncertain, despite a meta-regression analysis that found no clear relationship between aspirin dose and the risk of gastrointestinal GI) bleeding [5]. A recent task force publication addressed the use of aspirin for the primary prevention of ischemic stroke (3), but the recommendation for the use of aspirin for primary prevention of coronary heart disease (CHD) is less clear; and, the risk/benefit is perhaps an even more important consideration for primary compared to secondary prevention. The US Preventive Services Task Force estimates that for baseline risks of 1%, 3%, and 5%, 1–4, 4–12, and 6–20 CHD events can be avoided with aspirin primary prophylaxis, but at the risk of 0-2 hemorrhagic strokes and 2–4 major GI bleeds [3]. As primary prophylaxis, it is thus not clear at what risk levels the benefits of aspirin use outweigh its risks.

Ethnic and racial differences of aspirin for primary (and secondary) prevention are even less clear than aspirins use overall. For example, acute CHD mortality rates are twice as high in African Americans compared to whites with a larger disparity at younger ages, but little is known about the explanation for these differences. Since there are few reports on aspirin use for primary prevention of acute CHD, and even fewer by race, we examined these relationships in the REGARDS study, a large biracial national cohort.

## 2. MATERIALS AND METHODS

#### 2.1 Study Population

REGARDS is a national, population-based, biracial, longitudinal cohort study designed to examine underlying causes for racial and regional differences in stroke and CHD. The study oversampled African Americans (AAs) and persons living in the Stroke Belt region of the United States. Between January 2003 and October 2007, 30,239 individuals were enrolled, including 42% AA, 58% white, 45% men and 55% women. The sample includes 21% of participants from the Stroke Belt/Buckle, 35% from the Stroke Belt states, and the remaining 44% from the other 40 contiguous states. Participants were selected from commercially available lists (Genesys) based upon the above regions, and age of 45 years and over. A

brochure informed participants of the study and an upcoming phone call. During that call, verbal consent was obtained and a questionnaire was administered. The telephone response rate was 33%; the cooperation rate among those with confirmed eligibility was 49% (similar to the Multi-Ethnic Study of Atherosclerosis).

A participant was considered enrolled if they completed the telephone questionnaire and the in-person physical examination. Computer-assisted telephone interview (CATI) methods to collect demographic information and medical history were obtained by trained interviewers. Consent was obtained verbally by telephone and subsequently in writing during a follow-up in-home visit. The physical exam included anthropometric and blood pressure measurements, blood samples, and an electrocardiogram was conducted in-person, 3-4 weeks after the telephone interview. A medication inventory was conducted via pill bottle review at the time of the in-home visit. Self-administered questionnaires were left with the participant to gather further information. Participants were followed by telephone at sixmonth intervals and a report of a potential event triggered medical record retrieval; and reports of death triggered interviews with proxies in addition to retrieval of any hospital records that corresponded to a hospitalization near the time of death. The National Death Index was also queried. Study methods were reviewed and approved by all involved Institutional Review Boards. Additional methodological details are provided elsewhere [6]. For this analysis, the 5314 individuals with self-reported CHD at baseline (MI or coronary intervention) or evidence of MI on the baseline study ECG were excluded, since the focus was on primary prevention.

The primary dependent variable was incident acute CHD, defined as nonfatal or fatal events as adjudicated by a central panel of experts. Definitions of the outcomes were based on international consensus [7]. MI was classified as definite or probable if there was a biomarker (almost always troponin) rising or falling pattern with the peak twice the lowest listed upper limit of normal, plus at least one of the following: symptoms or signs suggestive of ischemia or EKG changes consistent with acute ischemia. If there were diagnostic EKG changes and ischemic signs or symptoms present but biomarkers were either unavailable or equivocal, the event was classified as probable MI. Acute CHD death was defined as definite fatal MI if death was within 28 days of hospital admission in definite MI cases, or postmortem findings consistent with MI within 28 days of death; while probable fatal MI was defined as death within 28 days of hospital admission in cases defined as probable MI; or death within 6 hours of hospital admission with cardiac symptoms and/or signs when other confirmatory data (biomarkers, ECG) were absent or not diagnostic. The designation of probable CHD death was applied to out-of-hospital cases of sudden cardiac death, or a death suggestive of acute CHD with a history of CHD and no other plausible cause of death. Outcomes that were analyzed included incident acute CHD, which included both fatal and nonfatal events, and fatal or nonfatal incident CHD were analyzed separately.

The primary independent variable was aspirin use. A participant was considered a "regular aspirin user" if they answered affirmatively to the question "Are you currently taking aspirin or aspirin containing products regularly, that is, at least two times each week?" Among these regular aspirin users, those answering affirmatively to: "For what purpose are you taking aspirin? Is it to reduce the chance of a heart attack or stroke?" were considered prophylactic

aspirin users for the primary analysis. Those answering affirmatively to the following question: "Is it to relieve pain?" And these participants were analyzed as aspirin users in a sensitivity analysis.

Factors considered as potentially confounding the relation between race and aspirin use were grouped into demographic measures, measures of socio-economic status, and cardiovascular risk factors. Demographic factors included age (defined in 10-year strata starting with age 45), race and gender. Measures of socio-economic status included annual household income and education (defined in strata, see Table 1). Cardiovascular risk factors included self-reported perceived health (on a 5-point scale from Poor to Excellent), hypertension (SBP 140mmHg, or DBP 90mmHg, or self-reported use of antihypertensive medications), diabetes (fasting glucose 126mg/dL or non-fasting glucose 200mg/dL or self-reported use of diabetes medications), dyslipidemia (total cholesterol 240mg/dL, low-density lipoprotein cholesterol 160mg/dL, high density lipoprotein cholesterol 40mg/dL or self-reported use of lipid lowering medications), smoking status (never, past, or current), and alcohol use (never, past, or current). Measures of medication adherence, were assessed by the validated Morisky scale\* [8].

We addressed confounding that could stem from individuals at highest risk possibly being the most motivated to take prophylactic aspirin. This potential confounding could result in subjects being categorized at high risk in analyses, so we conducted an analysis that examined risk by quartiles of the Framingham Coronary Heart Disease Risk Score (FRS) [9,10] which was used as a summary index of the CHD risk factor burden for each participant. This score reflects the 10-year probability of CHD given the individual's demographic and risk factor profile. The FRS includes age, sex, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density cholesterol, diabetes and current cigarette smoking.

#### 2.2 Statistical Analysis

The primary goal was to assess differences in risk for incident acute CHD by prophylactic aspirin usage. Univariate differences were tested using the chi-square test. To estimate the risk associated of treatment with prophylactic aspirin, we constructed Cox proportional hazards models to derive hazard ratios and 95% confidence intervals. Incremental models were used to test the impact that potential confounding variables had on any observed associations. We first adjusted for demographic factors (age, race, sex, and region), then adding indices of SES (income and education), then perceived general health, self-reported CVD risk factors (hypertension, diabetes, dyslipidemia, cigarette smoking and alcohol use), and finally the FRS.

To further assess the potential for a differential effect within patient subgroups (i.e., effect modification), we did a series of additional analyses, including an analysis stratified by FRS, race, and gender. We also analyzed risks associated with time to incident nonfatal and fatal acute CHD assessed separately, and an analysis where regular aspirin use for pain was included (Regular Aspirin Use-Table 1). Last, we examined time to all-cause mortality as a summary measure balancing risks and benefits. Statistical calculations were carried out with SAS version 9.2 (Cary, NC).

## 3. RESULTS

Of the total REGARDS sample, 5314 had a history or evidence of CHD at baseline and were excluded from the primary analysis. Sixteen individuals who did not answer the questions about aspirin use were excluded, and the 904 reported regularly taking aspirin for pain were excluded from the primary analysis. This left an analytic sample of 23,949. In multivariable analysis, other variables were missing in small numbers for each model {(model 1 consisted of 23493; model 2 of 23477, model 3 of 22101 and model 4 of 21918, (Fig. 1)}.

The characteristics of the study sample are shown in (Table 1). As can be seen, the number of users of aspirin for prophylaxis in the sample was 7883, or 33% of the total analyzable population. Also noted in this Table is that there were 503 acute incident CHD events.

The results of the primary multivariable analysis are presented in (Table 2). In all models, over a mean follow-up of 3.5 years (maximum 6 years) prophylactic aspirin use was not associated with incident acute CHD relative to no use. For the first model including only demographics, the hazard ratio (HR) was 1.05 (95% CI 0.86, 1.29). Adding socioeconomic indicators to this model had little impact on the HR. Beyond that, expected HRs for age, race, gender, income, level of education, diabetes, perceived health status etc. demonstrated expected trends.

In the analysis stratified by risk score, prophylactic aspirin use did not demonstrate any association with incident acute CHD (Table III). Of those using aspirin for prophylaxis, the majority (75%) was utilizing a low dose of 180 mg/d or less and, the use of low dose aspirin was slightly more common in whites (77.7%) than in African Americans (71.4%), and in women (78.8%) than men (71.4%). Use of low dose prophylactic aspirin was also more common among those of a higher socio-economic status (higher income and more education), those without diabetes or hypertension, never smokers, and current alcohol drinkers or those never having alcohol intake. Aspirin dose was similar among those with and without dyslipidemia (p>0.05). Subjects taking higher aspirin doses had higher Framingham Stroke and Coronary Heart Disease Risk Scores.

Sensitivity analysis that included the 904 subjects who reported taking regular aspirin for pain (rather than for prophylaxis), did not appreciably change the results (data not shown). However, in analyses stratified by FRS quartile, one unexpected finding was a higher incidence of acute CHD in low risk aspirin users. This latter unexpected finding, as well as the overall findings, held when we included all aspirin use, all-cause mortality, measures of medication adherence, and SBP. The findings did not differ by gender and diabetes status (tests of interaction were not significant). These findings were similar for fatal and nonfatal CHD analyzed separately, and for all-cause mortality (data not shown). Recent guidelines have suggested certain subsets that might benefit from prophylactic aspirin use such as women >65yo and women who are either high risk or diabetic. In these aforementioned subsets, aspirin did not affect the acute CHD endpoints.

The potential for aspirin to be associated with cerebral and gastrointestinal (GI) bleeding was also explored. On the CATI the question was asked "For each time you/he/she stayed as a patient in a hospital, nursing home or rehabilitation center, I need to know the reason, the

name and location of where you/he/she stayed, the date and the name of the doctor who treated you/him/her. Since we last spoke to you/him/her?

What was the reason you/he/she were/was admitted?

- 1. Stroke/brain aneurysm/TIA
- 2. Heart-related condition
- 3. Cancer
- 4. Other specify

If answered other, we searched the free text "other specify" response for the word "bleed" and then two of the authors classified each of the bleeds as a GI or not. For cerebral bleeds, the hospital records were centrally adjudicated by an expert committee, and no statistically significant difference was observed between aspirin users and non users. For GI bleeds (n=210), two models showed no difference but one model was borderline significant (p<. 0552).

## 4. DISCUSSION

In this large national cohort of subjects free of baseline CHD, we found no association between prophylactic aspirin use and incident acute CHD over a mean follow-up of 3.5 years. This lack of association was seen regardless of age, race, sex, degree of CHD risk factor burden, and a number of other demographic and baseline disease variables. Additional analyses examining risks associated with fatal incident events, and with all-cause mortality, revealed a similar lack of association. No excess hospitalized bleeding was observed in aspirin (mostly using low doses) vs. non aspirin users.

Since cardiovascular disease is the leading cause of death, efforts have been ongoing to identify interventions that contribute to CVD prevention [11]. The role of prophylactic aspirin use for the primary prevention of CHD is one such effort, but its use has not been convincingly established, although aspirin is approved for primary prevention in over 35 countries [12].

A recent meta-analysis concluded that primary prevention with aspirin decreased the risk for total cardiovascular events and nonfatal MI, but there were no significant differences in the incidence of stroke, CVD mortality, all-cause mortality or total CHD [13]. The 3 most recent studies in that meta-analysis were, for the most part inconclusive. Because of continued controversy regarding the exact role of prophylactic aspirin, there is an ongoing large clinical trial being conducted in a population at moderate risk of initial events, the Aspirin to Reduce Risk of Initial Vascular Events (ARRIVE) [4]. This latter study includes approximately 12,000 patients in seven countries and over 400 study sites. ARRIVE's aims are to demonstrate the efficacy and safety of low-dose (100-mg daily) aspirin in preventing first events associated with CVD in moderate risk individuals (defined as a 10–20% 10-year risk of a CHD event). Since many past trials assessed the role of aspirin in low risk subjects, and since we wanted to examine the role of confounding by baseline risk, we did stratify the analysis by baseline risk and found no association at any CHD risk level with one

exception-the finding that a higher incidence of acute CHD was observed in low risk aspirin users. Given the multiple analyses we conducted, it is possible that this exception is a chance result but it may be worthwhile to examine this in other cohorts.

Our study has several limitations worth noting. Some non-laboratory risk factors were based on self-report (although this is common to many epidemiologic studies), and individuals without telephones were necessarily excluded from selection into the study population. These excluded individuals may be of lower socioeconomic status and, therefore, may have different risk factor profiles than those included in this analysis. Also, the mean follow-up time of 3.5 years may not be long enough to have shown any benefit. Finally, participant usage of aspirin was also by self-report as was medication adherence.

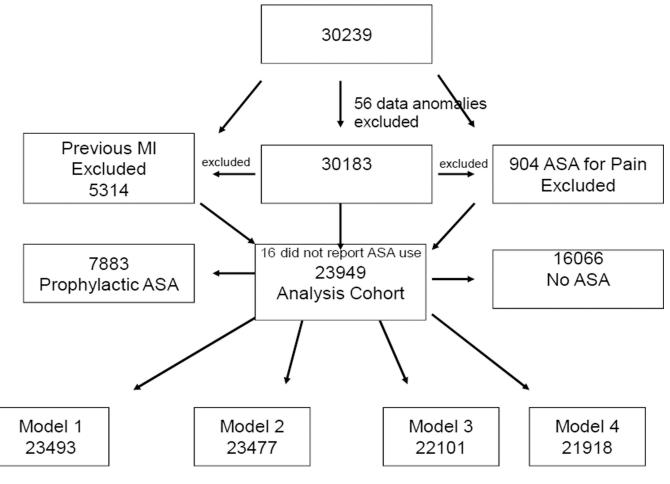
## 5. CONCLUSION

In conclusion, in this large national cohort study, we observed no association over a mean follow-up time of 3.5 years, between self-reported use of aspirin as primary prophylaxis in the prevention of incident acute CHD overall, nor on incident nonfatal or incident fatal acute CHD, or all-cause mortality. We also did not observe any excess hospitalized bleeding (cerebral or GI).

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**Fig. 1.** Exclusionary MI cascade

Table 1

Data broken down by prophylactic vs no aspirin use

| Table 1               | Overall |      | Not<br>prophylactic<br>aspirin user | actic<br>user | Prophylactic<br>aspirin user | ylactic<br>1 user | p-value<br>of<br>prophylactic<br>asnirin | Not regular<br>aspirin user | gular<br>user | Regular<br>aspirin<br>user | <b>1</b> - | p-value<br>of<br>regular<br>asnirin |
|-----------------------|---------|------|-------------------------------------|---------------|------------------------------|-------------------|--|-----------------------------|---------------|----------------------------|------------|-------------------------------------|
|                       | Z       | %    | Z                                   | %             | Z                            | %                 | users vs.<br>no                          | Z                           | %             | Z                          | %          | users<br>vs. no                     |
| Overall               | 23949   |      | 16066                               | 67.1          | 7883                         | 32.9              |  | 15506                       | 64.8          | 8443                       | 35.3       |                                     |
| Acute CHD             |         |      |                                     |               |                              |                   |  |                             |               |                            |            |                                     |
| No                    | 23446   | 97.9 | 15757                               | 67.2          | 7689                         | 32.8              | 0.0064                                   | 15213                       | 64.9          | 8233                       | 35.1       | 0.0021                              |
| Yes                   | 503     | 2.1  | 309                                 | 61.4          | 194                          | 38.6              |  | 293                         | 58.3          | 210                        | 41.8       |                                     |
| Mortality risk region | egion   |      |                                     |               |                              |                   |  |                             |               |                            |            |                                     |
| Low                   | 8083    | 33.8 | 5340                                | 66.1          | 2743                         | 33.9              | 0.0044                                   | 5160                        | 63.8          | 2923                       | 36.2       | 0.0073                              |
| Medium                | 8311    | 34.7 | 5547                                | 66.7          | 2764                         | 33.3              |  | 5346                        | 64.3          | 2965                       | 35.7       |                                     |
| High                  | 7525    | 31.5 | 5153                                | 68.5          | 2372                         | 31.5              |  | 4976                        | 66.1          | 2549                       | 33.9       |                                     |
| Race                  |         |      |                                     |               |                              |                   |  |                             |               |                            |            |                                     |
| Black                 | 10281   | 42.9 | 7259                                | 70.6          | 3022                         | 29.4              | <.0001                                   | 600L                        | 68.2          | 3272                       | 31.8       | <.0001                              |
| White                 | 13668   | 57.1 | 8807                                | 64.4          | 4861                         | 35.6              |  | 8497                        | 62.2          | 5171                       | 37.8       |                                     |
| Gender                |         |      |                                     |               |                              |                   |  |                             |               |                            |            |                                     |
| Male                  | 9866    | 41.7 | 6223                                | 62.3          | 3763                         | 37.7              | <.0001                                   | 5951                        | 59.6          | 4035                       | 40.4       | <.0001                              |
| Female                | 13963   | 58.3 | 9843                                | 70.5          | 4120                         | 29.5              |  | 9555                        | 68.4          | 4408                       | 31.6       |                                     |
| Age group             |         |      |                                     |               |                              |                   |  |                             |               |                            |            |                                     |
| 45-55                 | 3359    | 14.0 | 2751                                | 81.9          | 608                          | 18.1              | <.0001                                   | 2714                        | 80.8          | 645                        | 19.2       | <.0001                              |
| 55-65                 | 9598    | 40.1 | 6099                                | 68.9          | 2989                         | 31.1              |  | 6444                        | 67.1          | 3154                       | 32.9       |                                     |
| 65-75                 | 7375    | 30.8 | 4518                                | 61.3          | 2857                         | 38.7              |  | 4300                        | 58.3          | 3075                       | 41.7       |                                     |
| 75-85                 | 3223    | 13.5 | 1953                                | 60.6          | 1270                         | 39.4              |  | 1829                        | 56.8          | 1394                       | 43.3       |                                     |
| 85+                   | 394     | 1.6  | 235                                 | 59.6          | 159                          | 40.4              |  | 219                         | 55.6          | 175                        | 44.4       |                                     |
| Income                |         |      |                                     |               |                              |                   |  |                             |               |                            |            |                                     |
| <\$20K                | 4089    | 17.1 | 2811                                | 68.8          | 1278                         | 31.3              | 0.0002                                   | 2684                        | 65.7          | 1405                       | 34.4       | 0.0239                              |
| \$20K-\$35            | 5664    | 23.7 | 3807                                | 67.2          | 1857                         | 32.8              |  | 3676                        | 64.9          | 1988                       | 35.1       |                                     |
| \$35K-\$75K           | 7205    | 30.1 | 4857                                | 67.4          | 2348                         | 32.6              |  | 4703                        | 65.3          | 2502                       | 34.7       |                                     |
| \$75K+                | 3992    | 16.7 | 2559                                | 64.1          | 1433                         | 35.9              |  | 2495                        | 62.5          | 1497                       | 37.5       |                                     |

| N $\sqrt{6}$ N         N $\sqrt{6}$ N           | Table 1              | Overall | _    | Not<br>prophylactic<br>aspirin user | lactic<br>user | Prophylactic<br>aspirin user | Prophylactic<br>aspirin user | p-value<br>of<br>prophylactic<br>asnirin | Not regular<br>aspirin user | gular<br>user | Regular<br>aspirin<br>user | u u  | p-value<br>of<br>regular<br>asnirin |
|--|----------------------|---------|------|-------------------------------------|----------------|------------------------------|------------------------------|--|-----------------------------|---------------|----------------------------|------|-------------------------------------|
| 13040         10006         671         383         329         1550         648         843         55           income         299         12.5         2032         67.8         967         32.2         1948         65.0         1051         35.1           feducation         299         1.2.5         2032         67.8         967         32.2         1948         65.0         1051         35.1           feducation         2540         1.1.6         889         31.2          4178         66.0         35.3         35.3           biol         676         254         64.1         305         35.3  |                      | z       | %    | Z                                   | %              | z                            | %                            | users vs.<br>no                          | z                           | %             | Z                          | %    | users<br>vs. no                     |
| income         299         1.2         2032         6.7         3.2         7.0         1.948         6.0         1051         3.51           feduration          3         1         4         1         9         4         9         3.2         4017         6.0         1051         353           shool         780         1.16         1882         673         344         9         312         4017         666         2163         334           shool         7066         2.4         4179         688         32.3         4017         666         2163         334           off         3231         610         1317         310         00005         2333         375         375         375         375           off         4316         731         3118         1310         2037         531         373         375         375           off         4431         3461         373         323         373         375         375         375           off         4318         345         373         323         373         375         375         375           off         4318 <t< th=""><th>Overall</th><th>23949</th><th></th><th>16066</th><th>67.1</th><th>7883</th><th>32.9</th><th></th><th>15506</th><th>64.8</th><th>8443</th><th>35.3</th><th></th></t<>   | Overall              | 23949   |      | 16066                               | 67.1           | 7883                         | 32.9                         |  | 15506                       | 64.8          | 8443                       | 35.3 |                                     |
| FeducationSchool2780116188267.78983.23<0001  | Missing income       | 2999    | 12.5 | 2032                                | 67.8           | 967                          | 32.2                         |  | 1948                        | 65.0          | 1051                       | 35.1 |                                     |
| shool1780116188267.189832.3<0001178964.490135.7bool607625.4417968.813031.27401760.1203631.3olbes64337.1443868.8205531.27441760.1203631.3olbes64335.355.364.430.535.335.355.364.430.535.337.3old766332.157.364.337.337.327.337.337.337.3old766332.157.064.337.337.327.337.337.3301766332.157.064.337.337.337.337.337.3301766332.457.357.337.357.357.357.357.357.3301766332.477.357.337.357.357.357.357.357.330176332.477.357.337.357.357.357.357.357.357.357.357.330176377.357.377.357.3 <td>Years of educati</td> <td>ion</td> <td></td>   | Years of educati     | ion     |      |                                     |                |                              |                              |  |                             |               |                            |      |                                     |
| bold60%53.44176881331.2401764.120933.4ellege64321.144868.820531.241166.2216531.4ellege64335.953.464.430.935.67.231.231.231.3ellematin32.1510061.323.053.160.0283.167.335.3add766332.1510065.324.031.190.0283.167.335.331813.053.066.9217.833.190.0283.167.335.331813.050.353.066.3217.833.190.253.353.331813.150.353.066.937.333.190.223.354.441.331813.453.666.324.353.353.264.724.754.741.431813.453.663.333.353.254.354.741.441.431413.453.853.853.853.354.354.741.431413.413.453.853.853.750.953.754.741.431413.413.413.853.854.854.741.441.431413.413.413.754.331.754.754.741.431413.413.414.754  | < High School        | 2780    | 11.6 | 1882                                | 67.7           | 868                          | 32.3                         | <.0001                                   | 1789                        | 64.4          | 991                        | 35.7 | <.0001                              |
| ollege64327.1443668.820.531.2431866.621.633.4+83335.9553464.4305935.632.663.232.733.733.733.733.333.3ethenth33.3th32432.151.063.331.131.00000523.163.163.333.3odd766332.151.063.331.131.163.763.333.164.724.833.3131813.052.063.353.134.154.754.754.754.334.4131813.053.064.334.754.754.754.754.754.7131813.053.853.154.754.754.754.754.754.7131854.354.354.334.754.754.754.754.754.7131854.354.334.854.754.754.754.754.754.7131154.154.354.854.754.754.754.754.754.7131254.154.354.854.754.754.754.754.754.7131154.154.754.754.754.754.754.754.754.7131254.754.754.754.7<   | High School          | 6076    | 25.4 | 4179                                | 68.8           | 1897                         | 31.2                         |  | 4017                        | 66.1          | 2059                       | 33.9 |                                     |
| +893335.953.464.430.935.653.763.732.337.337.3eth tanth </td <td>Some College</td> <td>6483</td> <td>27.1</td> <td>4458</td> <td>68.8</td> <td>2025</td> <td>31.2</td> <td></td> <td>4318</td> <td>66.6</td> <td>2165</td> <td>33.4</td> <td></td>  | Some College         | 6483    | 27.1 | 4458                                | 68.8           | 2025                         | 31.2                         |  | 4318                        | 66.6          | 2165                       | 33.4 |                                     |
| ed healthit de localit32.151.00.0005283166.7141533.3it de localit32.151.067.355.063.058.155.058.335.4it de localit32.151.067.355.063.058.355.335.435.4it de localit33.151.067.355.333.153.264.6201935.4it de localit31.831.853.065.353.153.265.058.340.4it de localit51.051.038.333.157.359.659.657.340.4it de localit51.326.8351.326.953.759.657.340.4it de localit51.851.851.838.554.741.245.3it de localit51.851.851.851.850.053.754.754.7it de localit51.851.851.851.854.750.754.754.7it de localit51.851.851.851.854.754.754.754.7it de localit51.851.851.851.854.754.754.754.7it de localit51.851.851.851.854.754.754.754.7it de localit51.851.851.851.854.754.754.754.7it de localit51.851.851.8<   | College+             | 8593    | 35.9 | 5534                                | 64.4           | 3059                         | 35.6                         |  | 5370                        | 62.5          | 3223                       | 37.5 |                                     |
| tr $4246$ $178$ $2920$ $690$ $1317$ $31.0$ $0.0005$ $2831$ $66.7$ $1415$ $33.0$ $600$ $7663$ $32.1$ $5160$ $67.3$ $2503$ $32.1$ $4982$ $65.0$ $2681$ $35.0$ $8248$ $34.5$ $5520$ $66.9$ $2728$ $33.1$ $5329$ $64.6$ $2919$ $35.4$ $3118$ $130$ $2037$ $65.3$ $1081$ $34.7$ $240$ $38.3$ $772$ $2995$ $64.6$ $2919$ $37.4$ $626$ $2.6$ $386$ $61.7$ $240$ $38.3$ $57.7$ $1959$ $62.8$ $237.4$ $412$ $10435$ $43.7$ $7722$ $743$ $2883$ $57.7$ $2001$ $7560$ $72.5$ $2873$ $412$ $13461$ $56.3$ $8281$ $61.5$ $5180$ $38.5$ $7001$ $7560$ $5373$ $2976$ $2777$ $8$ $13461$ $56.3$ $8281$ $61.7$ $5180$ $38.5$ $7791$ $58.7$ $412$ $8$ $13461$ $56.3$ $8281$ $61.7$ $8001$ $7260$ $7250$ $5976$ $5976$ $5976$ $8$ $18507$ $8041$ $12777$ $690$ $5730$ $31.0$ $7001$ $12776$ $577$ $577$ $5971$ $5971$ $5971$ $8$ $11870$ $8181$ $5731$ $8192$ $5701$ $5916$ $5926$ $5926$ $5926$ $5926$ $5926$ $10245$ $5461$ $7282$ $7292$   | Perceived health     | _       |      |                                     |                |                              |                              |  |                             |               |                            |      |                                     |
| od 7663 3.1 5160 67.3 2503 32.7 4982 65.0 2681 35.0 35.4 432 83.1 5220 64.6 2919 35.4 33.1 5329 51.6 523 31.8 31.8 31.8 33.1 5329 64.6 2919 35.4 31.8 31.8 31.8 31.8 31.9 31.7 3539 64.5 233 40.4 31.8 31.8 31.8 31.8 31.7 31.8 31.8 31.9 31.9 31.8 31.8 31.8 31.8 31.8 31.9 31.9 31.8 31.8 31.8 31.8 31.8 31.8 31.8 31.8  | Excellent            | 4246    | 17.8 | 2929                                | 69.0           | 1317                         | 31.0                         | 0.0005                                   | 2831                        | 66.7          | 1415                       | 33.3 | 0.0006                              |
| 8248         34.5         5520         65.3         1081         33.1         5329         64.6         2919         35.4           3118         13.0         2037         65.3         1081         34.7         1959         62.8         1159         37.3           625         2.6         38.6         61.7         240         38.3         37.3         59.6         57.3         40.4           13461         56.3         8281         61.5         5180         38.5         7091         58.8         41.2           13461         56.3         8281         61.5         5180         38.5         7091         58.7         41.2           13461         56.3         8281         61.5         5180         38.5         54.7         41.2           13461         56.3         8281         61.5         5180         42.5         7756         58.7         41.2           13461         56.3         8291         61.5         5180         42.5         7756         54.7         41.2           13461         56.3         8291         61.2         72.5         54.7         2047         53.7         40.4           112750 <t< td=""><td>Very Good</td><td>7663</td><td>32.1</td><td>5160</td><td>67.3</td><td>2503</td><td>32.7</td><td></td><td>4982</td><td>65.0</td><td>2681</td><td>35.0</td><td></td></t<>   | Very Good            | 7663    | 32.1 | 5160                                | 67.3           | 2503                         | 32.7                         |  | 4982                        | 65.0          | 2681                       | 35.0 |                                     |
| 3118         13.0         50.3         65.3         1081         34.7         54.6         55.3         1159         57.5 <t< td=""><td>Good</td><td>8248</td><td>34.5</td><td>5520</td><td>60.9</td><td>2728</td><td>33.1</td><td></td><td>5329</td><td>64.6</td><td>2919</td><td>35.4</td><td></td></t<> | Good                 | 8248    | 34.5 | 5520                                | 60.9           | 2728                         | 33.1                         |  | 5329                        | 64.6          | 2919                       | 35.4 |                                     |
| 626         2.6         386         61.7         240         38.3         57.3         59.6         253         40.4           mision         10435         43.7         7752         74.3         2683         25.7         <0001   | Fair                 | 3118    | 13.0 | 2037                                | 65.3           | 1081                         | 34.7                         |  | 1959                        | 62.8          | 1159                       | 37.2 |                                     |
| inition1043543.7775274.3268325.7<0001756072.5287527.61043543.7775274.3268325.7<0001  | oor                  | 626     | 2.6  | 386                                 | 61.7           | 240                          | 38.3                         |  | 373                         | 59.6          | 253                        | 40.4 |                                     |
|  | <b>Hypertenision</b> |         |      |                                     |                |                              |                              |  |                             |               |                            |      |                                     |
| I3461         56.3         8281         61.5         5180         38.5         5547         41.2           s         1<  | No                   | 10435   | 43.7 | 7752                                | 74.3           | 2683                         | 25.7                         | <.0001                                   | 7560                        | 72.5          | 2875                       | 27.6 | <.0001                              |
| s         s           18507         80.4         12777         69.0         5730         31.0         <0001  | Yes                  | 13461   | 56.3 | 8281                                | 61.5           | 5180                         | 38.5                         |  | 7914                        | 58.8          | 5547                       | 41.2 |                                     |
|  | Diabetes             |         |      |                                     |                |                              |                              |  |                             |               |                            |      |                                     |
| 4519         19.6         2610         57.8         1909         42.2         2472         54.7         2047         45.3           lemia         1         2         2         2         2         2         2         4         45.3           lemia         1         1         2   | No                   | 18507   | 80.4 | 12777                               | 69.0           | 5730                         | 31.0                         | <.0001                                   | 12375                       | 6.99          | 6132                       | 33.1 | <.0001                              |
| lemia         73.0         2762         27.0         <0001         7219         70.5         3026         29.5           10245         44.6         7483         73.0         2762         27.0         <0001  | Yes                  | 4519    | 19.6 | 2610                                | 57.8           | 1909                         | 42.2                         |  | 2472                        | 54.7          | 2047                       | 45.3 |                                     |
| 10245         44.6         7483         73.0         27.62         27.0         <0001         7219         70.5         3026         29.5           12750         55.4         7876         61.8         4874         38.2         7597         59.6         5153         40.4           status         11232         47.5         61.8         4874         38.2         7597         59.6         5153         40.4           status         11322         47.5         61.8         38.8         31.7         <0001   | Dyslipidemia         |         |      |                                     |                |                              |                              |  |                             |               |                            |      |                                     |
| 12750         55.4         7876         61.8         4874         38.2         7597         59.6         5153         40.4           status         11322         47.5         7134         68.3         3588         31.7         <0001   | No                   | 10245   | 44.6 | 7483                                | 73.0           | 2762                         | 27.0                         | <.0001                                   | 7219                        | 70.5          | 3026                       | 29.5 | <.0001                              |
| status       11322       47.5       7734       68.3       3588       31.7       <.0001   | Yes                  | 12750   | 55.4 | 7876                                | 61.8           | 4874                         | 38.2                         |  | 7597                        | 59.6          | 5153                       | 40.4 |                                     |
| 11322         47.5         7734         68.3         35.88         31.7         <.0001         7486         66.1         3836         33.9           9126         38.3         5810         63.7         3316         36.3         5572         61.1         3554         38.9           3408         14.3         2454         72.0         954         28.0         23.82         69.9         1026         30.1           use           7354         30.7         5046         58.0         30.3         40.0         1026         30.1   | Smoke status         |         |      |                                     |                |                              |                              |  |                             |               |                            |      |                                     |
| 9126         38.3         5810         63.7         3316         36.3         5572         61.1         3554         38.9           3408         14.3         2454         72.0         954         28.0         2382         69.9         1026         30.1           use           7354         30.7         5046         68.6         2308         31.4         0.0005         4835         65.8         24.3         34.3  | Never                | 11322   | 47.5 | 7734                                | 68.3           | 3588                         | 31.7                         | <.0001                                   | 7486                        | 66.1          | 3836                       | 33.9 | <.0001                              |
| 3408         14.3         2454         72.0         954         28.0         2382         69.9         1026         30.1           use           7354         30.7         5046         68.6         2308         31.4         0.0005         4835         65.8         2519         34.3  | Past                 | 9126    | 38.3 | 5810                                | 63.7           | 3316                         | 36.3                         |  | 5572                        | 61.1          | 3554                       | 38.9 |                                     |
| <b>Ji use</b><br>7354 30.7 5046 68.6 2308 31.4 0.0005 4835 65.8 2519 34.3  | Current              | 3408    | 14.3 | 2454                                | 72.0           | 954                          | 28.0                         |  | 2382                        | 6.69          | 1026                       | 30.1 |                                     |
| 7354 30.7 5046 68.6 2308 31.4 0.0005 4835 65.8 2519 34.3   | Alcohol use          |         |      |                                     |                |                              |                              |  |                             |               |                            |      |                                     |
|  | Never                | 7354    | 30.7 | 5046                                | 68.6           | 2308                         | 31.4                         | 0.0005                                   | 4835                        | 65.8          | 2519                       | 34.3 | 0.0425                              |

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| Table 1                       | Overall      |       | Not<br>prophylactic<br>aspirin user | lactic<br>user | Proph.<br>aspirir | ylactic<br>1 user | Prophylactic p-value<br>aspirin user of<br>prophylactic | Not regular<br>aspirin user | gular<br>user | Regular<br>aspirin<br>user | ar   | p-value<br>of<br>regular<br>asnirin |
|-------------------------------|--------------|-------|-------------------------------------|----------------|-------------------|-------------------|---|-----------------------------|---------------|----------------------------|------|-------------------------------------|
|                               | Z            | %     | % N % N                             | %              |                   | %                 | users vs.<br>no   | z                           | % N           | z                          | %    | users<br>vs. no                     |
| Overall                       | 23949        |       | 16066 67.1 7883 32.9                | 67.1           | 7883              | 32.9              |   | 15506                       | 64.8          | 15506 64.8 8443 35.3       | 35.3 |                                     |
| Past                          | 4034         | 16.8  | 4034 16.8 2731 67.7 1303 32.3       | 67.7           | 1303              | 32.3              |   | 2628                        | 65.2          | 2628 65.2 1406 34.9        | 34.9 |                                     |
| Current                       | 12561 52.4   | 52.4  | 8289                                | 66.0 4272      | 4272              | 34.0              |   | 8043                        | 64.0          | 4518                       | 36.0 |                                     |
| Framingham cardiac risk score | cardiac risk | score |                                     |                |                   |                   |   |                             |               |                            |      |                                     |

<.0001

29.0 37.6 40.2 41.0

2468 2338 2074 1102

71.0 62.4 59.8

6032 3874 3081 1588

<.0001

27.3

2317 2184 1952 1001

72.7 64.8

6183 4028 3203 1689

37.7

8500 6212 5155 2690

0-5

27.5 22.9

37.9 35.2

37.2

62.8 62.1

11.9

10 - 205-10

20+

59.03

Table 2

Incremental analyses

| definite/probable<br>(definite/probable,<br>in-and out-of-<br>bospital), on/beforeHRLLULR tatal CHD<br>(definite/probable,<br>in-and out-of-<br>bospital), on/beforeHRLLULNospital), on/before<br>12/31/2008 $1.054$ $0.864$ $1.287$ Prophylactic aspirin vs. no $1.117$ $0.927$ $1.478$ MI high region vs. low $1.117$ $0.927$ $1.476$ MI high region vs. low $1.117$ $0.976$ $1.426$ MI high region vs. low $1.117$ $0.976$ $1.476$ Male vs. female $2.764$ $1.878$ $2.76$ 55-65 vs.45-55 $2.75$ $2.2536$ $1.676$ $3.847$ 55-65 vs.45-55 $2.845$ $2.76$ $3.845$ $2.909$ 65-75 vs.45-55 $3.845$ $2.766$ $3.845$ $2.76$ 55-65 vs.45-55 $3.845$ $2.766$ $3.845$ $2.76$ 55-65 vs.45-55 $3.845$ $2.766$ $3.845$ $2.766$ 55-65 vs.45-55 $3.845$ $2.766$ $3.845$ $2.766$ 55-65 vs.45-55 $3.845$ $2.766$ $3.845$ $2.766$ 55-65 vs.45-55 $3.845$ $2.766$ $1.676$ $3.847$ 55-75 vs.45-55 $3.845$ $2.766$ $1.676$ $1.676$ 55-75 vs.45-55 $3.845$ $3.845$ $2.845$ $1.67$ | HR<br>1.09<br>1.139<br>1.139<br>0.975<br>2.537<br>1.864<br>1.864<br>1.864<br>3.221<br>3.221<br>3.221 | LL<br>0.893<br>0.901<br>0.853 | nr    | HR    | ΓΓ    | П     | HR    | TL    | I       |
|---|--|-------------------------------|-------|-------|-------|-------|-------|-------|---------|
| in vs. no       1.054       0.864         in vs. low       1.17       0.927         .low       1.118       0.876         .low       1.118       0.876         1.175       0.965       1.175         2.264       1.858       1.241         2.264       1.858       1.241         2.264       1.858       2.468         2.20K       2.536       1.656         3.845       2.468       3.845       2.131         \$20K       2.50K       2.536       1.656         2.20K       3.845       2.168       3.845         2.01       2.536       1.556       3.845         2.01       2.536       1.556       3.845         2.01       2.536       1.556       3.845         2.01       2.536       1.556       3.845         2.01       2.536       1.556       3.845         2.01       3.845       2.468       3.845         2.01       3.845       2.468       3.845         2.01       3.845       2.468       3.845         2.11       3.845       2.468       3.845         3.10       3.845       3.84  | 1.09<br>1.139<br>1.089<br>0.975<br>2.537<br>1.864<br>1.864<br>3.221<br>3.221<br>3.518                | 0.893<br>0.901<br>0.853       |       |       |       |       |       |       | UL<br>D |
| in vs. no       1.054       0.864         n vs. low       1.17       0.927         . low       1.175       0.965         . low       1.175       0.965         1.175       0.965       1.858         2.264       1.858       1.241         2.264       1.858       1.241         2.264       1.858       3.845       2.468         2.20K       3.845       2.468       3.845       2.468         2.00K       2.536       1.656       3.845       2.468         2.01       2.536       1.656       3.845       2.468         2.01       2.536       1.656       3.845       2.468         2.01       2.536       1.656       3.845       2.468         2.01       2.536       1.656       3.845       2.468         2.01       2.536       1.656       1.656       3.845       1.656         2.01       2.536       2.661       1.656       1.656       1.656         2.01       2.530       2.661       2.661       1.656       1.656       1.656         2.11       2.131       2.131       2.131       1.666       1.656       1.656  | 1.09<br>1.139<br>1.189<br>0.975<br>2.537<br>1.864<br>1.864<br>2.278<br>3.221<br>3.221<br>3.518       | 0.893<br>0.901<br>0.853       |       |       |       |       |       |       |         |
| n vs. Jow       1.17       0.927         . Jow       1.118       0.876         . Jow       1.175       0.965         . 1.175       0.965       1.858         . 1.175       0.965       2.264         . 1.175       1.9       1.241         . 2.204       1.858       1.656         . 2.33       2.536       1.656         . 2.33       3.845       2.468         . 2.33       3.845       2.131         . 2.33       3.845       2.131         . 2.30K           . 2.30K           . 2.30K           . 2.30K  | 1.139<br>1.089<br>0.975<br>2.537<br>1.864<br>1.864<br>2.278<br>3.221<br>3.518                        | 0.901<br>0.853                | 1.331 | 0.998 | 0.81  | 1.23  | 1.073 | 0.872 | 1.321   |
| .low       1.10       0.876         1.175       0.965         2.264       1.858         1.9       1.241         2.336       1.656         3.845       2.468         3.845       2.468         3.845       2.131         \$20K       .         \$2.50K       .         \$2.50K <t< td=""><td>1.089<br/>0.975<br/>2.537<br/>1.864<br/>2.278<br/>3.218<br/>3.518</td><td>0.853</td><td>1.439</td><td>1.145</td><td>0.897</td><td>1.462</td><td>1.147</td><td>0.897</td><td>1.465</td></t<>                                     | 1.089<br>0.975<br>2.537<br>1.864<br>2.278<br>3.218<br>3.518  | 0.853                         | 1.439 | 1.145 | 0.897 | 1.462 | 1.147 | 0.897 | 1.465   |
| 1.175       0.965         2.264       1.858         2.264       1.858         1.9       1.241         2.536       1.656         3.845       2.468         3.845       2.463         3.845       3.845         3.845       3.845         3.845       3.845         3.84  | 0.975<br>2.537<br>1.864<br>2.278<br>3.221<br>3.518   |                               | 1.389 | 1.098 | 0.852 | 1.414 | 1.081 | 0.838 | 1.394   |
| 2.264       1.858         1.9       1.241         2.536       1.656         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       2.468         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.845       3.425         3.84  | 2.537<br>1.864<br>2.278<br>3.221<br>3.518  | 0.793                         | 1.198 | 0.785 | 0.629 | 0.981 | 0.858 | 0.689 | 1.068   |
| 1.9       1.241         2.536       1.656         3.845       2.468         3.845       2.468         3.845       2.131         \$20K       -         \$20K       - <tr td="">       -      <tr td=""></tr></tr>  | 1.864<br>2.278<br>3.221<br>3.518   | 2.07                          | 3.108 | 2.651 | 2.119 | 3.316 | 1.714 | 1.339 | 2.193   |
|   |  |                               |       |       |       |       |       |       |         |
|   |  |                               |       |       |       |       |       |       |         |
| 2.536       1.656         3.845       2.468         3.845       2.468         4.251       2.131         \$20K       -         \$2.131       -         \$2.131       -         \$2.131       -         \$2.00K       -         \$2.50K       -         \$2.50K       -         \$2.131       -         \$2.50K       - <td< td=""><td>2.278<br/>3.221<br/>3.518</td><td>1.217</td><td>2.855</td><td>2.095</td><td>1.305</td><td>3.363</td><td>1.664</td><td>1.03</td><td>2.687</td></td<>  | 2.278<br>3.221<br>3.518  | 1.217                         | 2.855 | 2.095 | 1.305 | 3.363 | 1.664 | 1.03  | 2.687   |
| 3.845       2.468         4.251       2.131         \$20K       -       -         \$20K       -       -         \$20K       -       -       -         \$20K       -       -       -         \$20K       -       -       -       -         \$5.50K       -       -       -       -       -         \$5.50K       -   | 3.221<br>3.518   | 1.482                         | 3.504 | 2.712 | 1.678 | 4.384 | 1.813 | 1.105 | 2.977   |
| 4.251       2.131         \$20K       .       .         \$3< \$20K  | 3.518  | 2.051                         | 5.06  | 3.954 | 2.392 | 6.537 | 2.248 | 1.326 | 3.81    |
| \$20K-\$35K vs.< \$20K  |  | 1.751                         | 7.069 | 4.4   | 2.027 | 9.554 | 2.122 | 0.955 | 4.716   |
| \$35K-\$75K vs<\$20K  | 0.807  | 0.612                         | 1.064 | 0.858 | 0.642 | 1.145 | 0.87  | 0.651 | 1.162   |
| \$75K+ vs.<\$20K  | 0.578  | 0.425                         | 0.786 | 0.658 | 0.477 | 0.907 | 0.676 | 0.49  | 0.933   |
| Missing income vs.< \$20K   | 0.607  | 0.413                         | 0.892 | 0.75  | 0.498 | 1.129 | 0.782 | 0.518 | 1.181   |
| High school graduate vs. less than high school graduate       .   | 0.666  | 0.467                         | 0.948 | 0.69  | 0.473 | 1.008 | 0.705 | 0.483 | 1.03    |
| some college vs. less than high school  | 0.663  | 0.489                         | 0.899 | 0.743 | 0.541 | 1.02  | 0.772 | 0.562 | 1.062   |
| college graduate vs. less than high school Very good health vs. excellent   | 0.51   | 0.366                         | 0.712 | 0.667 | 0.47  | 0.947 | 0.689 | 0.485 | 0.98    |
| Very good health vs. excellent<br>Good health vs. excellent<br>Tair health vs. excellent  | 0.914  | 0.679                         | 1.231 | 0.998 | 0.73  | 1.364 | 1.048 | 0.765 | 1.436   |
| Good health vs. excellent   |  |                               |       | 0.906 | 0.646 | 1.272 | 0.941 | 0.671 | 1.32    |
| Eair haalth ve avrallant  |  |                               |       | 1.202 | 0.866 | 1.669 | 1.288 | 0.931 | 1.78    |
|   |  |                               |       | 1.576 | 1.081 | 2.298 | 1.746 | 1.206 | 2.526   |
| Poor health vs. excellent   |  |                               |       | 1.988 | 1.146 | 3.449 | 2.186 | 1.269 | 3.765   |
| Hypertensive vs. not  |  |                               |       | 1.42  | 1.128 | 1.788 | 0.93  | 0.75  | 1.154   |
| Diabetic vs. not  |  |                               |       | 1.521 | 1.208 | 1.915 |       |       |         |
| Dyslipidemic vs. not  |  |                               |       | 1.043 | 0.843 | 1.29  | 1.092 | 0.86  | 1.388   |
| Past Smoker vs. never   |  |                               |       | 1.104 | 0.869 | 1.401 | 1.097 | 0.802 | 1.501   |

| Incident acute<br>nonfatal<br>(definite/nrobable)  | Demo | Demographics | 70 | Demo | Demo+SES |       | Demo  | +SES+CI | D+RF        | Demo+SES+CD+RF Demo+SES+CD+RF<br>+FH | SES+CI      | )+RF  |
|--|------|--------------|----|------|----------|-------|-------|---------|-------------|--------------------------------------|-------------|-------|
| OR fatal CHD<br>OR fatal CHD<br>(definite/probable,<br>in- and out-of-<br>hospital), on/before<br>12/31/2008 | H    | ΓΓ           | UL | HR   | ΓΓ       | TT NT | HR    | П       | Tn          | 逬                                    | TT          | l     |
| Current smoker vs. never   |      |              |    |      |          |       | 1.704 | 1.267   | 2.291       | 1.704 1.267 2.291 0.991 0.764 1.287  | 0.764       | 1.287 |
| Current alcohol vs. never  |      |              |    |      |          |       | 0.957 |         | 0.737 1.242 | 1.244                                | 1.244 0.927 | 1.67  |
| Past alcohol vs. never   |      |              |    |      |          |       | 1.198 |         | 0.894 1.607 | 2.221                                | 1.522       | 3.242 |
| CHD risk quart 2 vs. 1   |      |              |    |      |          |       |       |         |             | 3.162                                | 2.145       | 4.661 |
| CHD risk quart 3 vs. 1   |      |              |    |      |          |       |       |         |             | 4.915                                | 3.204       | 7.54  |
| CHD risk quart 4 vs. 1   |      |              |    |      |          |       |       |         |             | 5.193                                | 2.995       | 9.004 |

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Time to incident acute nonfatal (definite/probable) or fatal CHD (definite/probable\*), stratified by risk score

| actor nomata<br>(definite/probable) OR<br>fatal<br>(definite/probable, in-<br>and out-of-hospital),<br>anth-of-rea 12/31/2008 | prophyls<br>region, r | prophylactic aspirin,<br>region, race, gender, age | n,<br>r, age   | model 1+income,<br>education   | income,<br>n   |                | Model 3<br>model 2+dyslipi<br>hypertensive, dii<br>self reported hee<br>drinking status,<br>smoking status | Model 3<br>model 2-dyslipidemic,<br>hypertensive, diabetic,<br>self reported health,<br>drinking status,<br>smoking status | nic,<br>etic,<br>1, |
|---|-----------------------|--|----------------|--|----------------|----------------|--|--|---------------------|
| stratified by risk  | [   V****             | hazard rat   | ios and li     | ****All hazard ratios and limits are prophylatic aspirin users vs. not | ophylatic      | aspirin us     | ers vs. not  |  |                     |
|   | Hazard<br>Ratio       | Hazard Lower<br>Ratio Limit                        | Upper<br>Limit | Upper Hazard Lower<br>Limit Ratio Limit                                | Lower<br>Limit | Upper<br>Limit | Hazard Lower<br>Ratio Limit  | Lower<br>Limit   | Upper<br>Limit      |
| CHD risk score 20+  | 1.189                 | 0.825  | 1.714          | 1.218  | 0.845          | 1.756          | 1.187  | 0.823  | 1.713               |
| CHD risk score 10–20  | 0.714                 | 0.49   | 1.04           | 0.739  | 0.507          | 1.078          | 0.691  | 0.471  | 1.014               |
| CHD risk score 5-10   | 1.126                 | 0.741  | 1.712          | 1.136  | 0.748          | 1.727          | 1.078  | 0.708  | 1.642               |
| CHD risk score 0–5  | 2.008                 | 1.083  | 3.725          | 2.002  | 1.079          | 3.713          | 1.963  | 1.049  | 3.672               |