

SEX DIFFERENCES IN HEALTH STATUS AFTER ACUTE MYOCARDIAL INFARCTION

BY  
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## ***Abstract***

**Background:** Past research suggests that women, as compared with men, have worse survival after an acute myocardial infarction (AMI). However, little is known about whether women also have worse health status (symptoms, function, and quality of life [QOL]) after an AMI.

**Methods:** Across two multi-centered AMI registries (PREMIER and TRIUMPH), we examined whether there were sex differences in health status recovery among 4,555 AMI patients using the validated disease-specific Seattle Angina Questionnaire (SAQ). We compared 1-year change in SAQ angina frequency and QOL scores for men and women with hierarchical linear regression models that adjusted for demographics, clinical comorbidities, socio-economic factors, and medication treatment. To facilitate interpretability, we also compared the presence of any angina as a dichotomous variable at 1 year (SAQ angina frequency score <100 vs. 100).

**Results:** Of 4,555 AMI patients, 1,481(32.5%) were women. Women were older, more frequently of black race and widowed, and were more likely to have economic barriers to care, including financial difficulty affording medications and be unemployed. Compared with men, women had lower mean baseline ( $61.3\pm 23.4$  vs.  $64.9\pm 22.7$ ) and 1-year ( $80.3\pm 21.5$  vs.  $84.2\pm 19.0$ ) QOL scores, and less model-adjusted improvement in QOL at 1-year ( $-2.60$  SAQ points; 95% CI:  $-1.31, -3.90$ ;  $P<0.001$ ). Although women and men had similar baseline SAQ angina scores ( $85.0\pm 20.7$  vs.  $85.8\pm 20.4$ ), women had more frequent angina at 1-year ( $91.6\pm 17.6$  vs.  $94.1\pm 14.9$ ), which resulted in less model-adjusted improvement in angina frequency scores after adjustment for all covariates ( $-2.85$  SAQ points; 95% CI:  $-1.34, -4.36$ ;  $P<0.001$ ). This also translated to a 28% increased odds of any angina at 1-year (adjusted OR=1.28; 95% CI = 1.07, 1.52;  $P=0.01$ ).

**Conclusion:** Compared with men, women have worse health status recovery after AMI than men, with smaller improvements in QOL and angina symptoms at 1 year.

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## **INTRODUCTION:**

Although women are known to have lower rates of survival after an acute myocardial infarction (AMI) than men, which is largely explained by differences in age and clinical comorbidities<sup>1</sup>, it is unknown whether women also have worse quality of life and more frequent angina after AMI, even after adjusting for clinical, socioeconomic, and psychological factors that are known to differ by sex. Determining whether sex differences exist for not only traditional ‘hard’ clinical end points (e.g., death and readmission) but also for health status (symptoms, quality of life) is important because these latter outcomes affect patients’ burden of illness, are increasingly recognized as important patient-centered outcomes in clinical studies, and are potentially modifiable through additional anti-anginal therapy or coronary revascularization.<sup>2,3</sup>

To date, most prior studies on AMI have typically collected information on ‘hard’ clinical end points, such as death and recurrent AMI, or have used generic health status instruments to assess patients’ health status. However, generic instruments are less informative than disease-specific health status instruments as the former lack information on whether patients continue to be burdened by symptoms specific to their disease, such as angina after AMI.<sup>4</sup> The emergence of the Seattle Angina Questionnaire (SAQ)<sup>5</sup>—a disease-specific instrument for patients with coronary artery disease, which has been shown to be reliable, valid, responsive to clinical change, and prognostic of mortality, provides a unique opportunity to assess whether women, in addition to having lower survival, also have worse health status outcomes after AMI.

To address this gap in knowledge, we leveraged health status data from two large multi-centered AMI registries that contained detailed information on patients’ health status, economic status, and psychosocial factors. We were thus able to adjust for a range of differences between men and women to examine whether patient’s sex was independently associated with disease-specific

health status recovery (change in quality of life and residual angina) 1 year after AMI. If differences exist, we sought to further identify which patient and treatment factors may explain sex differences in these health status outcomes. We also examined whether there was an interaction between patients' age and sex to determine whether sex differences in health status recovery was prevalent for both younger (less than 55 years) and older patients (greater than 55 years). Results from these analyses can inform our understanding of the extent and potential mediators of sex differences in outcomes for patients with an AMI.

## **METHODS:**

### ***Study Population and Data Sources***

We used data from two US-based, multi-center, prospective, observational registries of consecutive AMI patients—the TRIUMPH<sup>6</sup> (Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status) and PREMIER<sup>7</sup> (Prospective Registry Evaluating Outcomes After Myocardial Infarctions: Events and Recovery) registries, which enrolled AMI patients from 2003 through 2008. Specifically, from 2003-04, 2498 MI patients from 19 U.S. hospitals were enrolled in PREMIER, and between 2005-08, 4340 MI patients from 24 U.S. hospitals were enrolled in TRIUMPH (12 hospitals participated in both registries). Both studies employed similar data collection processes and collected similar data elements, enabling pooling of their results.

Briefly, patients in both studies were eligible for inclusion if they were 18 years or older, had elevated cardiac enzymes (troponins or creatinine kinase-MB) within 24 hours of hospital admission and had supporting evidence suggestive of AMI, including either prolonged ischemic symptoms or electrocardiographic ST-changes. Exclusion criteria included patients who were incarcerated, refused participation, were unable to provide consent, did not speak English or Spanish, were transferred to the participating hospital from another facility >24 hours after initial admission, or expired prior to being contacted by the investigators. Demographic, social, clinical, health status and psychological data for patients were collected from chart abstraction and baseline interviews by trained staff within 24 to 72 hours of the index AMI admission. All participating patients provided informed consent, and the study protocol was approved by the institutional review board at each participating center.

A total of 6838 AMI patients were enrolled in PREMIER (n = 2498) and TRIUMPH (n = 4340). Because we were interested in examining health status outcomes of patients at 1-year after hospital discharge, we excluded 41 patients who were missing baseline QOL scores and 2,242 patients who did not have a health status outcome assessment at 1-year (477 patients died prior to the 1-year follow-up and 1765 did not complete a 1-year health status assessment). Our final study cohort comprised 4555 AMI patients (Figure 1).

### ***Health Status Outcomes***

The primary outcomes in this study were angina and quality of life. These were measured using the disease-specific Seattle Angina Questionnaire (SAQ)—a validated, reliable, and responsive health status instrument for patients with coronary artery disease that has been shown to be prognostic of future mortality, readmissions for acute coronary syndrome, and costs.<sup>4, 5, 8-10</sup> For this study, we focused on the SAQ Angina Frequency and Quality of Life domains, as these likely represent the most important health status domains for patients. Patient responses to the SAQ were translated for each domain onto a scale from 0 to 100, with higher scores indicating less frequent angina and better quality of life. We evaluated 1-year scores for each domain, as well as health status recovery (1-year *improvement* in angina and quality of life). Finally, to facilitate the clinical interpretability of the SAQ Angina Frequency scale, we also dichotomized this scale into any (SAQ Angina Frequency score <100) or no (SAQ Angina Frequency score = 100) angina.

### ***Study variables***

The key independent variable in this study was patients' sex. In addition, both PREMIER and TRIUMPH collected information on age and race (white, black, and other). Clinical and treatment

variables were collected and included medical comorbidities (chronic lung disease, chronic kidney disease, congestive heart failure, diabetes, hypercholesterolemia, hypertension, peripheral arterial disease, prior angina, prior MI, prior percutaneous coronary intervention [PCI] or coronary artery bypass surgery [CABG], prior stroke), and smoking history. Information on AMI severity were also obtained including Killip class (class I/II vs. III/IV), and type of AMI (ST elevation vs. non-ST elevation). The registries also collected detailed data on socioeconomic factors and depression<sup>11, 12</sup>, as these are important potential confounders of the relationship between patients' sex and health status outcomes. Socioeconomic factors included marital, perceived social support, depression, insurance coverage, employment status, and perceived financial difficulties. Perceived social support was measured by the 5-item Enhancing Recovery In Coronary Heart Disease (ENRICHD) Social Support Inventory (ESSI). Based on prior work, low social support was defined as a score of  $\leq 3$  on 2 or more items (excluding items on instrumental social support and marital status) and having a sum score of  $\leq 18$  on the remaining 5 items.<sup>13</sup> Depressive symptoms were assessed using the validated Patient Health Questionnaire (PHQ-8).<sup>14</sup> PHQ-8 scores range from 0 to 24, with higher scores denoting more severe symptoms and a score of  $\geq 10$  defining major depression.<sup>14</sup> Financial difficulties were assessed during the structured interviews by asking patients the severity of the economic burden of medical costs (severe, moderate, somewhat, little, no burden) and if they avoided obtaining medical care due to costs.<sup>15</sup>

Finally, data on AMI treatment was collected, including medications at discharge (beta-blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, aspirin, and statin therapy) and whether the patient was treated with coronary revascularization (PCI or CABG) during the index hospitalization.

### *Statistical analysis*

Baseline characteristics between women and men were compared using Student t-tests for continuous variables and the chi-square test for categorical variables. We also compared baseline and 1-year SAQ quality of life and angina frequency scores between women and men using Student's t-tests, and evaluated for crude differences in health status recovery (i.e., change in SAQ quality of life and angina frequency scores at 1 year) using paired t-tests.

To examine the extent that any observed sex differences in health status recovery (SAQ Angina Frequency and Quality of Life scores) were explained by differences in (1) demographics (age and race), (2) clinical factors (comorbidities and severity of MI), (3) socioeconomic and psychological factors (marital and employment status, educational level attained, insurance coverage, perceived financial difficulties, social support, and depression), and (4) AMI treatment (medications at discharge and also whether the patient was treated with coronary revascularization during the hospital stay), we constructed sequential hierarchical logistic regression models, to account for clustering by site, for each health status measure and adjusted for each of these domains in a cumulative fashion. Baseline SAQ scores were included in all models. In these models, patient data were nested within hospitals, and hospitals were modeled as random effects, while the aforementioned variables were modeled as fixed effects.<sup>16</sup> We evaluated the degree to which sex differences in health status recovery (i.e., improvement in SAQ quality of life and angina frequency scores) were attenuated with adjustment for each of these classes of factors and whether sex differences persisted even after full model adjustment for all observed factors. Finally, we examined for an interaction between patients' age ( $\leq 55$  vs.  $> 55$ ) and sex in the final models. There was very little missing data in the registries; missing covariates were imputed with 5 imputation data sets

using IVEware (Imputation and Variance Estimation Software; University of Michigan's Survey Research Center, Institute for Social Research, Ann Arbor, MI).

All analyses were conducted with SAS Version 9.2 (SAS Institute, Cary, NC), IVEWARE (University of Michigan, MI),<sup>17</sup> and R Version 2.6.0 (Free Software Foundation, Boston, MA).<sup>18</sup> All tests for statistical significance were two-tailed and evaluated at a significance level of 0.05.

## **RESULTS:**

We compared patients who were previously excluded to our study cohort (Table 1). Of the 2283 missing patients, 775 (33.9%) were women. Missing cohort was mostly non-Caucasian, younger, and did not have health insurance. Of the 4,555 patients in the cohort, 1,481(32.5%) were women (Table 2). Women were older and more frequently of black race. Clinically, women were less likely to have an ST elevation MI but higher MI severity (i.e., higher Killip class) during the index hospitalization. They were also more likely to have co-existing chronic lung disease, diabetes mellitus, hypertension, but were less likely to have prior angina, MI, and coronary revascularization (Table 2). Women were more frequently widowed, and were more likely to be unemployed, have more severe depressive symptoms, and have economic barriers to care, including financial difficulty affording medications (Table 2). Finally, women were less likely to be discharged on a beta blocker, aspirin, and statin for their AMI, and they were also less likely to be treated with coronary revascularization (PCI or CABG) during their index hospitalization. (Table 2)

### *Quality of Life*

Compared with men, women had lower baseline QOL scores ( $61.3 \pm 23.4$  vs.  $64.9 \pm 22.7$ ;  $P < 0.001$ ). At 1 year, women continued to have lower QOL scores. In unadjusted models, 1-year change in QOL scores was similar between men and women (absolute difference of  $-0.39$  [95% CI:  $-1.98$  to  $1.19$ ]). However, after adjustment for baseline QOL scores and other demographics, women had a 4-point lower improvement in QOL scores than men at 1 year ( $-4.13$  [95% CI:  $-2.94$  to  $-5.31$ ]) (Figure 2). These sex differences were essentially unchanged after adjustment for clinical comorbidities and AMI severity and were only modestly attenuated after full adjustment, including for sex differences in socioeconomic factors, psychological factors, and AMI

treatment, (-2.60 [95% CI: -3.90 to -1.31]  $P<0.001$ ). Lastly, there was no interaction between patients' age ( $\leq 55$  vs.  $>55$ ) and sex in 1-year change in QOL ( $P$  for interaction of 0.68), suggesting that both younger and older women had worse 1-year improvement in QOL than similarly aged men.

### *Angina*

At their index hospitalization for AMI, women and men had similar baseline SAQ angina frequency scores ( $85.0 \pm 20.7$  vs.  $85.8 \pm 20.4$ ;  $P=0.21$ ). By 1-year follow-up, however, women had significantly lower angina frequency scores ( $91.6 \pm 17.6$  vs.  $94.1 \pm 14.9$ ;  $P<0.001$ ) (see Table 3). In unadjusted models, women had a slightly, but non-significantly, lower improvement in angina scores at 1 year compared with men (difference in 1-year change in angina frequency scores between women and men: -1.58 [95% CI: -2.97 to -0.20]). This sex difference in improvement in SAQ angina frequency scores at 1 year widened after adjustment for baseline angina frequency score and demographics, and did not meaningfully change after even after full adjustment for clinical, socioeconomic factors, psychological factors, and AMI treatment, (-2.85 [95% CI: -4.36 to -1.34];  $P<0.001$ ) (Figure 3). There was no interaction between patients' age ( $\leq 55$  vs.  $>55$ ) and sex in 1-year change in angina ( $P$  for interaction of 0.14). Importantly, when 1-year achieved angina scores was evaluated as a dichotomous variable of any vs. no angina at 1 year, women had a 27% increased odds of having any angina at 1-year (adjusted Odds Ratio: 1.28 [95% CI: 1.07 to 1.52;  $P=0.001$ ) (Figure 4).

## **DISCUSSION:**

In this multi-site study of AMI patients, we found that women have worse 1-year health status after AMI than men, with smaller improvements in both QOL and angina than men. These differences persisted even after adjusting for numerous demographics, clinical comorbidities, AMI severity and treatment. For the outcome of change in 1-year change in QOL, additional adjustment for socioeconomic and psychological factors modestly attenuated (~40% narrowing, from -4.1 points to -2.6 points) sex differences in 1-year improvement in QOL scores, although there remained less improvement in QOL among women than men. In contrast, for 1-year angina frequency, further adjustment for socioeconomic confounders, psychological factors, and AMI treatment did not attenuate sex differences. While the clinical importance of a 3 to 5 point difference on the SAQ may not be particularly intuitive, we also found this difference in SAQ improvement translated into a 28% greater likelihood of women having angina at 1-year after an AMI as compared with men. Collectively, our findings highlight that women have less robust improvements in QOL and angina symptoms after an incident AMI, even after accounting for non-clinical factors known to be influential in sex-based research.

Many prior studies have examined sex differences in mortality after AMI. Indeed, a recent systematic review identified 39 studies which presented data on mortality after AMI for men and women and found that, although most of these studies reported higher unadjusted mortality rates for women compared with men, sex differences were largely attenuated after adjustment for differences in age and clinical characteristics.<sup>1</sup>

In contrast, few studies have examined the association of patients' sex and health status after AMI. Wiklund et al. surveyed 595 AMI survivors two decades ago and found that women had higher rates of psychological and psychosomatic complaints (especially sleep disturbances) one year

after their AMI.<sup>19</sup> Emery et al. followed 410 patients with a variety of cardiac diseases for one year and found that women had lower QOL on the SF-36, compared with men.<sup>20</sup> Xu et al. reported that women have less improvement in QOL at 1-month after AMI using the Euro-Qol utility index.<sup>21</sup> None of these studies, however, used a disease-specific instrument to assess patients' health status after AMI or adjusted for important socioeconomic and psychological confounders of the association between sex and health status. More recently, in a multi-center registry of AMI patients  $\leq 55$  years of age and younger, Dreyer et al. found that women had worse baseline and 1-year health status than men but similar absolute improvements in SAQ scores between baseline and 1-year.<sup>22</sup> Our study extends the work of these investigators by examining sex differences in health status *improvement* in QOL and angina symptoms after AMI in all AMI patients, regardless of age. We found that, compared with men, women had significantly less improvement in QOL and angina symptoms 1-year after their AMI, even after adjusting for a wide variety of potentially confounding demographic, clinical, socioeconomic, psychological, and AMI treatment. Moreover, our interaction analyses suggest that sex differences in health status recovery was prevalent for both younger patients ( $\leq 55$ ) and older ( $>55$ ) patients.

An important finding in this study was that the baseline differences in age, race, and clinical comorbidities between men and women did not explain our findings of sex differences in health status recovery after AMI. Although women were older, were more frequently of black race, had a higher Killip class, and had higher rates of chronic lung disease, diabetes mellitus, and hypertension than men, adjustment for these factors did not narrow sex differences in 1-year improvements in QOL or angina. This stands in contrast to mortality<sup>1</sup>, wherein differences in age and clinical factors have been found to mediate much of the raw mortality differences between men and women. Adjustment for certain socioeconomic and psychological factors, such as educational and

employment status, financial difficulties with accessing medical care, and social support, did reduce by ~40% sex differences in QOL improvement after AMI but had no impact on sex differences in improvement in angina symptoms. However, it remains unclear whether these factors are easily modifiable by interventions. Finally, although sex differences in discharge medication treatment and coronary revascularization existed, these were not found to be mediators of sex differences in health status recovery for either QOL or angina.

Our study should be interpreted in the context of the following potential limitations. Although we were able to account for a rich variety of clinical and non-clinical confounders not typically collected in sex disparities research, the possibility of residual confounding remains, given that our study was observational in nature. Second, we detected only modest sex differences in 1-year recovery of QOL and angina. However, this difference of 3 to 5 points in SAQ scores is comparable to the clinical benefit obtained from percutaneous coronary intervention as compared with medical therapy in randomized trials and is therefore meaningful.<sup>23</sup> Finally, we were unable to assess the factors underlying residual sex differences in 1-year improvement in QOL and angina, even after adjustment for a number of important confounders. Whether these residual differences represent differences in reporting of health status recovery between men and women, unmeasured treatments (e.g., sex differences in outpatient care or use of cardiac rehabilitation), or unmeasured sex differences in clinical, social, and economic factors remains unknown and is worthy of further study.

After an AMI, women have worse health status recovery than men, with lower quality of life and more frequent angina. Although some of this is explained by social, economic, and psychological factors, there remain sex differences in the trajectory of health status improvement after adjusting for these factors as well as AMI treatment. Since we did find that women were less

likely to receive coronary revascularization and evidenced-based medications after AMI, greater attention is needed to ensure that this gap in treatment is eliminated to ensure that women have the best chance to achieve optimal health status improvement after their AMI.

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**Table 1: Patient Characteristics**

|                             | Total<br>n = 6838 | Missing<br>n = 2283 | Study cohort<br>n = 4555 | p-value |
|-----------------------------|-------------------|---------------------|--------------------------|---------|
| <b>Demographics</b>         |                   |                     |                          |         |
| Sex                         |                   |                     |                          | 0.234   |
| Male                        | 4582 (67.0%)      | 1508 (66.1%)        | 3074 (67.5%)             |         |
| Female                      | 2256 (33.0%)      | 775 (33.9%)         | 1481 (32.5%)             |         |
| Age                         | 59.7 ± 12.6       | 58.4 ± 13.5         | 60.4 ± 12.1              | < 0.001 |
| Race                        |                   |                     |                          | < 0.001 |
| White/Caucasian             | 4499 (66.5%)      | 1215 (53.9%)        | 3284 (72.7%)             |         |
| Black/African American      | 1644 (24.3%)      | 775 (34.4%)         | 869 (19.2%)              |         |
| Other                       | 627 (9.2%)        | 263 (11.7%)         | 364 (8.1%)               |         |
| Missing                     | 68                | 30                  | 38                       |         |
| <b>Comorbidities</b>        |                   |                     |                          |         |
| Chronic Lung Disease        | 648 (9.5%)        | 260 (11.4%)         | 388 (8.5%)               | < 0.001 |
| Chronic Renal Failure       | 573 (8.4%)        | 268 (11.7%)         | 305 (6.7%)               | < 0.001 |
| Congestive Heart Failure    | 674 (9.9%)        | 334 (14.6%)         | 340 (7.5%)               | < 0.001 |
| Diabetes                    | 2056 (30.1%)      | 785 (34.4%)         | 1271 (27.9%)             | < 0.001 |
| Hypercholesterolemia        | 3352 (49.0%)      | 1054 (46.2%)        | 2298 (50.5%)             | < 0.001 |
| Hypertension                | 4483 (65.6%)      | 1576 (69.0%)        | 2907 (63.8%)             | < 0.001 |
| Peripheral Arterial Disease | 399 (5.8%)        | 151 (6.6%)          | 248 (5.4%)               | 0.051   |
| Prior Angina                | 1087 (15.9%)      | 367 (16.1%)         | 720 (15.8%)              | 0.774   |
| Prior MI                    | 1449 (21.2%)      | 572 (25.1%)         | 877 (19.3%)              | < 0.001 |
| Prior PCI                   | 1298 (19.0%)      | 468 (20.5%)         | 830 (18.2%)              | 0.023   |
| Prior CABG                  | 818 (12.0%)       | 281 (12.3%)         | 537 (11.8%)              | 0.532   |
| Prior CVA or Prior TIA      | 516 (7.5%)        | 200 (8.8%)          | 316 (6.9%)               | 0.007   |
| History of Smoking          | 4118 (60.2%)      | 1445 (63.3%)        | 2673 (58.7%)             | < 0.001 |
| <b>MI Characteristics</b>   |                   |                     |                          |         |
| MI Killip Class             |                   |                     |                          | < 0.001 |
| I                           | 5557 (86.8%)      | 1786 (83.3%)        | 3771 (88.5%)             |         |
| II                          | 659 (10.3%)       | 280 (13.1%)         | 379 (8.9%)               |         |
| III                         | 123 (1.9%)        | 62 (2.9%)           | 61 (1.4%)                |         |
| IV                          | 65 (1.0%)         | 17 (0.8%)           | 48 (1.1%)                |         |
| Unknown                     | 434               | 138                 | 296                      |         |

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**Psychosocial factors**

|                             |              |             |              |         |
|-----------------------------|--------------|-------------|--------------|---------|
| Marital Status              |              |             |              | < 0.001 |
| Married                     | 3663 (54.0%) | 976 (43.2%) | 2687 (59.3%) |         |
| Divorced                    | 1122 (16.5%) | 417 (18.5%) | 705 (15.6%)  |         |
| Widowed                     | 809 (11.9%)  | 311 (13.8%) | 498 (11.0%)  |         |
| Single (never married)      | 768 (11.3%)  | 355 (15.7%) | 413 (9.1%)   |         |
| Other                       | 427 (6.3%)   | 198 (8.8%)  | 229 (5.1%)   |         |
| Missing                     | 49           | 26          | 23           |         |
| ENRICH Social Support Score | 21.9 ± 4.5   | 21.4 ± 5.0  | 22.2 ± 4.2   | < 0.001 |
| Missing                     | 211          | 92          | 119          |         |
| PHQ Depression Score        | 5.4 ± 5.4    | 5.9 ± 5.7   | 5.1 ± 5.3    | < 0.001 |
| Missing                     | 415          | 181         | 234          |         |

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**Economic factors**

|                                    |              |              |              |         |
|------------------------------------|--------------|--------------|--------------|---------|
| No health insurance                | 1250 (18.9%) | 551 (24.9%)  | 699 (15.8%)  | < 0.001 |
| Insurance coverage for medications | 4929 (73.4%) | 1487 (66.8%) | 3442 (76.7%) | < 0.001 |
| Economic burden of medical costs   |              |              |              | < 0.001 |
| Severe burden                      | 712 (10.6%)  | 286 (12.9%)  | 426 (9.5%)   |         |
| Moderate burden                    | 632 (9.4%)   | 227 (10.2%)  | 405 (9.0%)   |         |
| Somewhat burden                    | 726 (10.8%)  | 261 (11.8%)  | 465 (10.3%)  |         |
| Little burden                      | 619 (9.2%)   | 194 (8.7%)   | 425 (9.4%)   |         |
| No burden at all                   | 4031 (60.0%) | 1252 (56.4%) | 2779 (61.8%) |         |
| Missing                            | 118          | 63           | 55           |         |
| Avoided healthcare due to cost     | 1530 (22.9%) | 603 (27.3%)  | 927 (20.7%)  | < 0.001 |
| Not taken medication due to cost   |              |              |              | < 0.001 |
| Always                             | 174 (2.6%)   | 81 (3.6%)    | 93 (2.1%)    |         |
| Frequently                         | 346 (5.1%)   | 147 (6.6%)   | 199 (4.4%)   |         |
| Occasionally                       | 530 (7.9%)   | 218 (9.8%)   | 312 (6.9%)   |         |
| Rarely                             | 427 (6.3%)   | 164 (7.4%)   | 263 (5.8%)   |         |
| Never                              | 5270 (78.1%) | 1619 (72.6%) | 3651 (80.8%) |         |
| Missing                            | 91           | 54           | 37           |         |
| Employment status                  |              |              |              | 0.001   |
| Full-time                          | 2558 (37.8%) | 797 (35.5%)  | 1761 (39.0%) |         |
| Part-time                          | 614 (9.1%)   | 189 (8.4%)   | 425 (9.4%)   |         |
| Unemployed                         | 3589 (53.1%) | 1261 (56.1%) | 2328 (51.6%) |         |
| Missing                            | 77           | 36           | 41           |         |

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**AMI Treatment**

|                                |              |              |              |         |
|--------------------------------|--------------|--------------|--------------|---------|
| Beta Blocker                   | 6070 (89.3%) | 1957 (87.3%) | 4113 (90.3%) | < 0.001 |
| ACE or ARB                     | 5024 (73.9%) | 1684 (75.1%) | 3340 (73.3%) | 0.114   |
| Aspirin                        | 6344 (93.3%) | 2059 (91.8%) | 4285 (94.1%) | < 0.001 |
| Statin                         | 5811 (85.5%) | 1890 (84.3%) | 3921 (86.1%) | 0.049   |
| Revascularization: PCI or CABG | 4960 (72.5%) | 1465 (64.2%) | 3495 (76.7%) | < 0.001 |

**Table 2: Baseline Characteristics of the Study Cohort**

|                             | <b>Total<br/>(n=4555)</b> | <b>Male<br/>(n=3074)</b> | <b>Female<br/>(n=1481)</b> | <b>P value</b> |
|-----------------------------|---------------------------|--------------------------|----------------------------|----------------|
| <b>Demographics</b>         |                           |                          |                            |                |
| Age                         | 60.4 ± 12.1               | 59.3 ± 11.5              | 62.6 ± 12.9                | < 0.001        |
| Race                        |                           |                          |                            | < 0.001        |
| White                       | 3284 (72.7%)              | 2339 (76.7%)             | 945 (64.4%)                |                |
| Black                       | 869 (19.2%)               | 447 (14.7%)              | 422 (28.8%)                |                |
| Other                       | 364 (8.06%)               | 264 (8.66%)              | 100 (6.82%)                |                |
| Missing                     | 38                        | 24                       | 14                         |                |
| <b>Comorbidities</b>        |                           |                          |                            |                |
| Chronic lung disease        | 388 (8.5%)                | 215 (7.0%)               | 173 (11.7%)                | < 0.001        |
| Chronic renal failure       | 305 (6.7%)                | 207 (6.7%)               | 98 (6.6%)                  | 0.88           |
| Congestive heart failure    | 340 (7.5%)                | 214 (7.0%)               | 126 (8.5%)                 | 0.06           |
| Diabetes                    | 1271 (27.9%)              | 785 (25.5%)              | 486 (32.8%)                | < 0.001        |
| Hypercholesterolemia        | 2298 (50.5%)              | 1573 (51.2%)             | 725 (49.0%)                | 0.16           |
| Hypertension                | 2907 (63.8%)              | 1845 (60.0%)             | 1062 (71.7%)               | < 0.001        |
| Peripheral Arterial Disease | 248 (5.4%)                | 157 (5.1%)               | 91 (6.1%)                  | 0.15           |
| Prior Angina                | 720 (15.8%)               | 509 (16.6%)              | 211 (14.2%)                | 0.05           |
| Prior MI                    | 877 (19.3%)               | 618 (20.1%)              | 259 (17.5%)                | 0.04           |
| Prior PCI                   | 830 (18.2%)               | 601 (19.6%)              | 229 (15.5%)                | < 0.001        |
| Prior CABG                  | 537 (11.8%)               | 397 (12.9%)              | 140 (9.5%)                 | < 0.001        |
| Prior CVA or Prior TIA      | 316 (6.9%)                | 196 (6.4%)               | 120 (8.1%)                 | 0.03           |
| History of Smoking          | 2673 (58.7%)              | 1915 (62.3%)             | 758 (51.2%)                | < 0.001        |
| <b>MI Characteristics</b>   |                           |                          |                            |                |
| MI Killip Class             |                           |                          |                            | 0.002          |
| I                           | 3771 (88.5%)              | 2578 (89.8%)             | 1193 (86.0%)               |                |
| II                          | 379 (8.9%)                | 222 (7.7%)               | 157 (11.3%)                |                |
| III                         | 61 (1.4%)                 | 39 (1.4%)                | 22 (1.6%)                  |                |
| IV                          | 48 (1.1%)                 | 33 (1.1%)                | 15 (1.1%)                  |                |
| Unknown                     | 296                       | 202                      | 94                         |                |
| ST-elevation MI             | 2062 (45.3%)              | 1483 (48.2%)             | 579 (39.1%)                | < 0.001        |

|                                    | <b>Total<br/>(n=4555)</b> | <b>Male<br/>(n=3074)</b> | <b>Female<br/>(n=1481)</b> | <b>P value</b> |
|------------------------------------|---------------------------|--------------------------|----------------------------|----------------|
| <b>Psychosocial factors</b>        |                           |                          |                            |                |
| Marital Status                     |                           |                          |                            | < 0.001        |
| Married                            | 2687 (59.3%)              | 2067 (67.6%)             | 620 (42.1%)                |                |
| Divorced                           | 705 (15.6%)               | 428 (14.0%)              | 277 (18.8%)                |                |
| Widowed                            | 498 (11.0%)               | 155 (5.1%)               | 343 (23.3%)                |                |
| Single (never married)             | 413 (9.1%)                | 267 (8.7%)               | 146 (9.9%)                 |                |
| Other                              | 229 (5.1%)                | 142 (4.6%)               | 87 (5.9%)                  |                |
| Missing                            | 23                        | 15                       | 8                          |                |
| ENRICH Social Support Score        | 22.2 ± 4.2                | 22.3 ± 4.1               | 22.0 ± 4.2                 | 0.03           |
| Missing                            | 119                       | 84                       | 35                         |                |
| PHQ Depression Score               | 5.1 ± 5.3                 | 4.6 ± 4.9                | 6.3 ± 5.7                  | < 0.001        |
| Missing                            | 234                       | 145                      | 89                         |                |
| <b>Economics factors</b>           |                           |                          |                            |                |
| No health insurance                | 699 (15.8%)               | 481 (16.2%)              | 218 (15.1%)                | 0.35           |
| Insurance coverage for medications | 3442 (76.7%)              | 2377 (78.6%)             | 1065 (72.9%)               | < 0.001        |
| Economic burden of medical costs   |                           |                          |                            | 0.001          |
| Severe burden                      | 426 (9.5%)                | 254 (8.4%)               | 172 (11.8%)                |                |
| Moderate burden                    | 405 (9.0%)                | 272 (9.0%)               | 133 (9.1%)                 |                |
| Somewhat burden                    | 465 (10.3%)               | 299 (9.8%)               | 166 (11.3%)                |                |
| Little burden                      | 425 (9.4%)                | 287 (9.5%)               | 138 (9.4%)                 |                |
| No burden at all                   | 2779 (61.8%)              | 1925 (63.4%)             | 854 (58.4%)                |                |
| Missing                            | 55                        | 37                       | 18                         |                |
| Avoided healthcare due to cost     | 927 (20.7%)               | 594 (19.6%)              | 333 (22.8%)                | 0.02           |
| Employment Status                  |                           |                          |                            | < 0.001        |
| Full-time                          | 1761 (39.0%)              | 1397 (45.9%)             | 364 (24.8%)                |                |
| Part-time                          | 425 (9.4%)                | 285 (9.4%)               | 140 (9.5%)                 |                |
| Unemployed                         | 2328 (51.6%)              | 1362 (44.7%)             | 966 (65.7%)                |                |
| Missing                            | 41                        | 30                       | 11                         |                |
| Not taking medications due to cost |                           |                          |                            | < 0.001        |
| Always                             | 93 (2.1%)                 | 56 (1.8%)                | 37 (2.5%)                  |                |
| Frequently                         | 199 (4.4%)                | 118 (3.9%)               | 81 (5.5%)                  |                |
| Occasionally                       | 312 (6.9%)                | 180 (5.9%)               | 132 (9.0%)                 |                |
| Rarely                             | 263 (5.8%)                | 158 (5.2%)               | 105 (7.2%)                 |                |
| Never                              | 3651 (80.8%)              | 2538 (83.2%)             | 1113 (75.8%)               |                |
| Missing                            | 37                        | 24                       | 13                         |                |

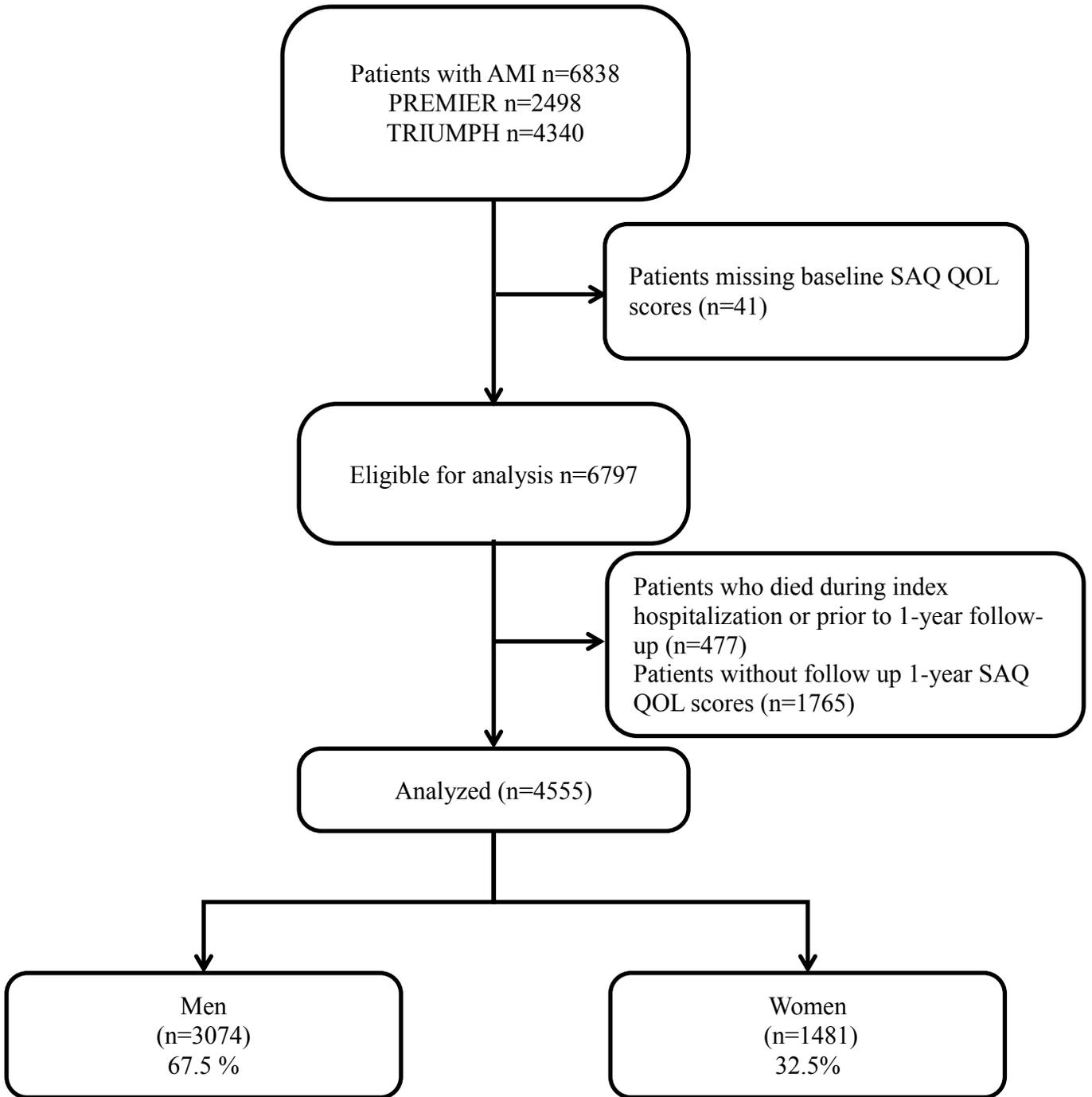
|                                | <b>Total<br/>(n=4555)</b> | <b>Male<br/>(n=3074)</b> | <b>Female<br/>(n=1481)</b> | <b><i>P</i> value</b> |
|--------------------------------|---------------------------|--------------------------|----------------------------|-----------------------|
| <b>AMI Treatment</b>           |                           |                          |                            |                       |
| Beta Blocker                   | 4113 (90.3%)              | 2794 (90.9%)             | 1319 (89.1%)               | 0.05                  |
| ACE-I or ARB                   | 3340 (73.3%)              | 2279 (74.1%)             | 1061 (71.6%)               | 0.07                  |
| Aspirin                        | 4285 (94.1%)              | 2918 (94.9%)             | 1367 (92.3%)               | < 0.001               |
| Statin                         | 3921 (86.1%)              | 2701 (87.9%)             | 1220 (82.4%)               | < 0.001               |
| Revascularization:             |                           |                          |                            |                       |
| PCI or CABG (primary or other) | 3495 (76.7%)              | 2485 (80.8%)             | 1010 (68.2%)               | < 0.001               |

Abbreviations: ENRICHD = Enhancing Recovery In Coronary Heart Disease; PHQ = Patient Health Questionnaire; ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker

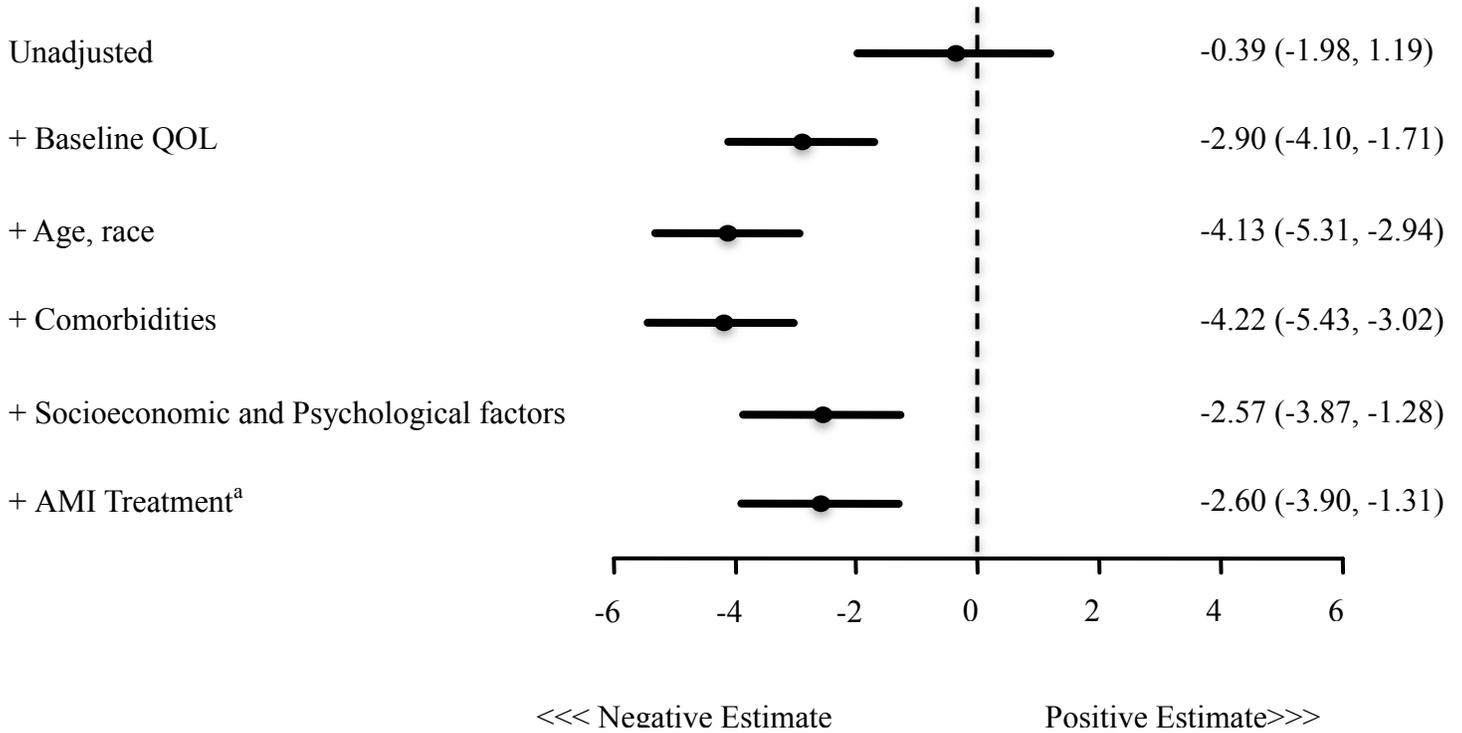
**Table 3: Baseline and 1-Year Health Status By Sex**

|                      | <b>Total</b><br>(n=4555) | <b>Male</b><br>(n=3074) | <b>Female</b><br>(n=1481) | <b>P value</b> |
|----------------------|--------------------------|-------------------------|---------------------------|----------------|
| <b>Baseline</b>      |                          |                         |                           |                |
| SAQ Quality of Life  | 63.8 ± 23.0              | 64.9 ± 22.7             | 61.3 ± 23.4               | < 0.001        |
| SAQ Angina Frequency | 85.6 ± 20.5              | 85.8 ± 20.4             | 85.0 ± 20.7               | 0.21           |
| <b>12-month</b>      |                          |                         |                           |                |
| SAQ Quality of Life  | 83.0 ± 19.9              | 84.2 ± 19.0             | 80.3 ± 21.5               | < 0.001        |
| SAQ Angina Frequency | 93.3 ± 15.8              | 94.1 ± 14.9             | 91.6 ± 17.6               | < 0.001        |
| Any angina at 1-year | 21%                      | 19.7%                   | 25.7%                     | < 0.001        |

**Figure 1: Flowchart of analytic cohort**



**Figure 2. Sex Difference in 1-Year QOL Health Recovery.\*** At 1 year, women had less improvement in 1-year disease-specific QOL scores than men.

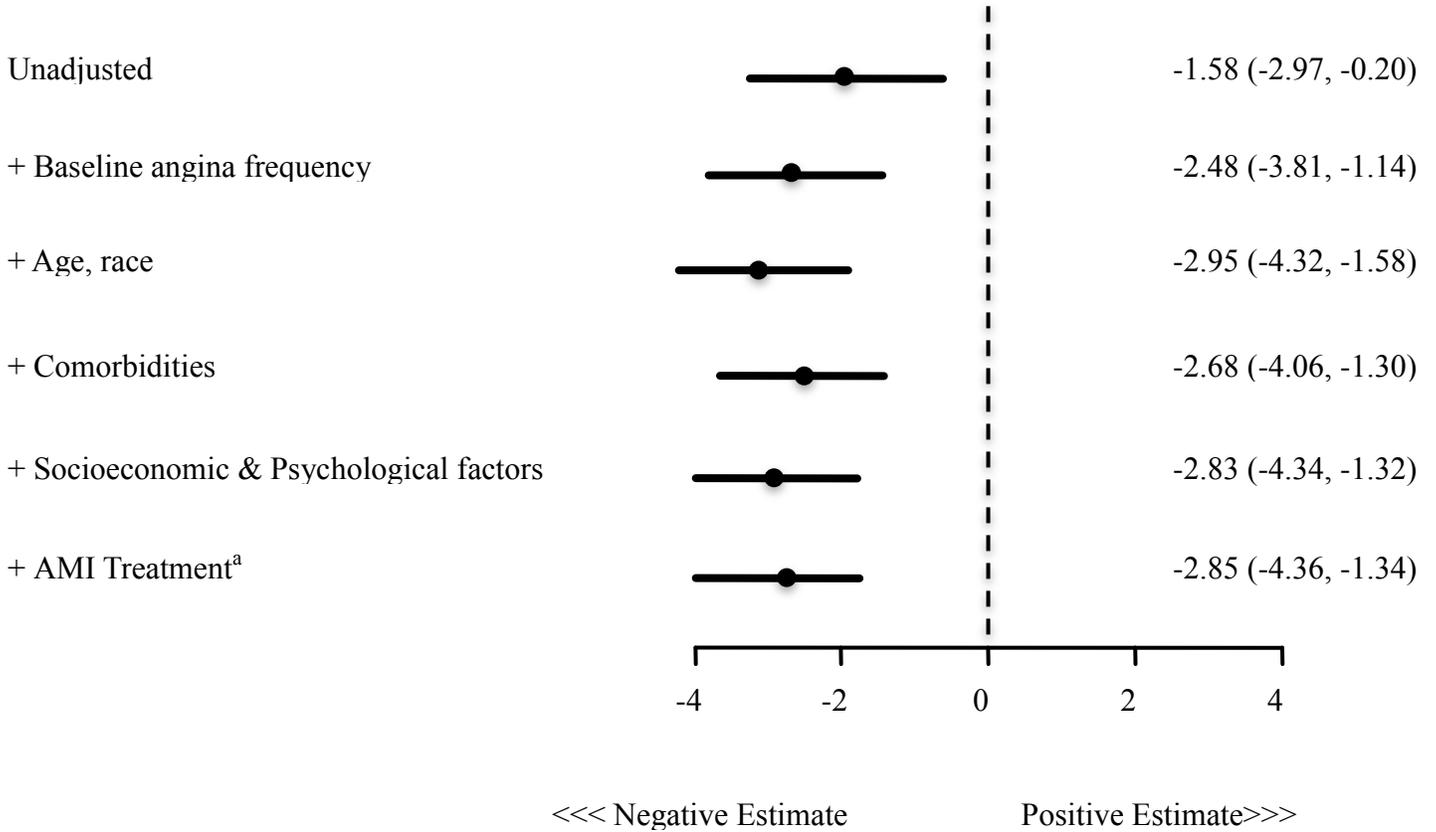


\*A negative estimate suggests that women had less improvement in 1-year QOL scores on the SAQ, whereas a positive estimate suggests that women had greater improvement.

<sup>a</sup>AMI treatment refers to medication at discharge and whether the patient was treated with coronary revascularization during the hospital stay

Abbreviations: QOL, quality of life.

**Figure 3. Sex Difference in 1-Year Angina Frequency Health Recovery.\*** At 1 year, women had less improvement in 1-year disease-specific angina frequency scores than men.



\*A negative estimate suggests that women had less improvement in 1-year angina frequency scores on the SAQ, whereas a positive estimate suggests that women had greater improvement.

<sup>a</sup>AMI treatment refers to medication at discharge and whether the patient was treated with coronary revascularization during the hospital stay

