Depressive symptoms in younger women and men with acute myocardial infarction

Smolderen, K.G.E.; Strait, Kelly M.; Dreyer, Rachel P.; D'Onofrio, Gail; Zhou, Shengfan; Lichtman, Judith H.; Geda, Mary; Bueno, Hector; Beltrame, John; Safdar, Basmah; Krumholz, Harlan M.; Spertus, John A.

Published in:
Journal of the American Heart Association

DOI:
10.1161/JAHA.114.001424

Publication date:
2015

Document Version
Publisher's PDF, also known as Version of record

Link to publication in Tilburg University Research Portal

Citation for published version (APA):
Smolderen, K. G. E., Strait, K. M., Dreyer, R. P., D'Onofrio, G., Zhou, S., Lichtman, J. H., Geda, M., Bueno, H., Beltrame, J., Safdar, B., Krumholz, H. M., & Spertus, J. A. (2015). Depressive symptoms in younger women and men with acute myocardial infarction: Insights from the VIRGO Study. Journal of the American Heart Association, 4(4), [e001424]. https://doi.org/10.1161/JAHA.114.001424

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.
Depressive Symptoms in Younger Women and Men With Acute Myocardial Infarction: Insights From the VIRGO Study

Kim G. Smolderen, PhD; Kelly M. Strait, MS; Rachel P. Dreyer, PhD; Gail D’Onofrio, MD, MS; Shengfan Zhou, MS; Judith H. Lichtman, PhD, MPH; Mary Geda, MSN; Héctor Bueno, MD, PhD; John Beltrame, MD; Basmah Safdar, MD, MSc; Harlan M. Krumholz, MD, SM; John A. Spertus, MD, MPH

Background—Depression was recently recognized as a risk factor for adverse medical outcomes in patients with acute myocardial infarction (AMI). The degree to which depression is present among younger patients with an AMI, the patient profile associated with being a young AMI patient with depressive symptoms, and whether relevant sex differences exist are currently unknown.

Methods and Results—The Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study enrolled 3572 patients with AMI (67.1% women; 2:1 ratio for women to men) between 2008 and 2012 (at 103 hospitals in the United States, 24 in Spain, and 3 in Australia). Information about lifetime history of depression and depressive symptoms experienced over the past 2 weeks (Patient Health Questionnaire; a cutoff score ≥10 was used for depression screening) was collected during index AMI admission. Information on demographics, socioeconomic status, cardiovascular risk, AMI severity, perceived stress (14-item Perceived Stress Scale), and health status (Seattle Angina Questionnaire, EuroQol 5D) was obtained through interviews and chart abstraction. Nearly half (48%) of the women reported a lifetime history of depression versus 1 in 4 in men (24%; P<0.0001). At the time of admission for AMI, more women than men experienced depressive symptoms (39% versus 22%; P<0.0001; adjusted odds ratio 1.64; 95% CI 1.36 to 1.98). Patients with more depressive symptoms had higher levels of stress and worse quality of life (P<0.01). Depressive symptoms were more prevalent among patients with lower socioeconomic profiles (eg, lower education, uninsured) and with more cardiovascular risk factors (eg, diabetes, smoking).

Conclusions—A high rate of lifetime history of depression and depressive symptoms at the time of an AMI was observed among younger women compared with men. Depressive symptoms affected those with more vulnerable socioeconomic and clinical profiles. (J Am Heart Assoc. 2015;4:e001424 doi: 10.1161/JAHA.114.001424)

Key Words: acute myocardial infarction • depression • sex differences

Young women aged <60 years who present with an acute myocardial infarction (AMI) have an elevated risk of mortality compared with men of that age group.1–2 A potential mediator of their poor outcomes might be depressive symptoms, which occur in ~1 of every 3 patients with AMI3 and have been shown to be associated with detrimental long-term outcomes.4–6 Although the nature and causality of the mechanisms that might explain the association between depressive symptoms and adverse prognosis in cardiac disease have not been established, both biological (eg, increased inflammation, inflammatory imbalance, increased platelet reactivity) and behavioral (eg, smoking, obesity, poor medication adherence) mechanisms have been proposed.7 Among depressed patients with AMI, some subpopulations...
may be particularly vulnerable to adverse outcomes.4,8 Prior studies have suggested that demographic characteristics can identify higher risk patients (e.g., depressive symptoms are present in 40% of women aged ≤60 years, whereas 1 in 5 men in that age group report having depressive symptoms).4,8 The need for further work to confirm and extend the existing literature on the most vulnerable patients (e.g., young women)4 is underscored by the latest scientific statement issued by the American Heart Association, which elevated depression to the status of an official risk factor in cardiac disease.6 A significant gap remains in the knowledge about prevalence and correlates of significant depressive symptoms among young patients presenting with an AMI. Identifying subtypes and characteristics of depression among young patients with AMI can lay the foundation for developing novel targeted treatments for depression in this group of patients.

The Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study was designed to examine the risk factors and outcomes for young patients recovering from an AMI.5 The goals of this study were (1) to evaluate the degree to which depressive symptom burden (lifetime history and depressive symptoms assessed during AMI admission) is present among younger patients with AMI; (2) to examine the demographic, socioeconomic, and clinical patient profiles associated with being a young AMI patient and having concomitant depressive symptoms; and (3) to examine the association between sex and depressive symptoms in AMI patients, independent of other risk factors. Being able to address these goals could inform a more actionable approach in risk-stratifying young men and women with AMI who are at risk of experiencing depressive symptoms. We hypothesized that female patients and those with more unfavorable socioeconomic and clinical profiles would suffer from a higher depression burden. Being able to address these aims would allow us to identify key areas of focus for younger AMI patients in designing plans for better prevention, identification, and treatment of their depressive symptoms. In addition, this study may also identify important characteristics that differ by sex that might confound sex-based differences between outcomes in younger patients with AMI.

Methods

Participants

Patients 18 to 55 years old with AMI were recruited into the VIRGO study between August 21, 2008, and January 5, 2012, from 103 hospitals in the United States, 24 in Spain, and 3 in Australia using a 2:1 ratio of women to men for enrollment. The methods of VIRGO have been described previously.9 In brief, patients were eligible for the study if they had increased cardiac biomarkers (i.e., myocardial necrosis needed to be present or at least 1 of the following markers needed to be elevated: troponin I or T level >99th percentile of the upper reference limit or creatine kinase level greater than twice the upper reference limit with creatine kinase-MB activity level >10% total) and at least 1 of the following conditions: symptoms of ischemia or electrocardiographic changes indicative of new ischemia (new ST-T changes, new or presumably new left bundle branch block, or the development of pathological Q waves). Only patients who presented directly or who were transferred to the enrolling site within the first 24 hours of presentation were eligible. Patients who were incarcerated; who did not speak English or Spanish; who were unable to provide informed consent or to be contacted for follow-up; or who developed elevated cardiac markers as a result of elective coronary revascularization, physical trauma, or surgery were excluded. An overview of the actual reasons for exclusion is provided in Table S1. Institutional review board approval was obtained at each participating center, and all patients provided informed consent for their study participation.

Data Collection and Variables

Baseline hospitalization data were collected by medical chart abstraction, and standardized in-person interviews were administered by trained personnel during admission for AMI or shortly thereafter (92% were performed in the hospital, 8% were conducted within 3 days of discharge) (Table S2). Depressive symptoms and health status data were collected through the baseline interview.

Information about depression consisted of self-reported lifetime history of depression collected at the time of the in-person interview (“Have you ever in your life been told you have depression or been treated for depression by a doctor or other health care provider?” [yes or no]) and current symptoms of depression assessed with the 9-item version of the Patient Health Questionnaire (PHQ-9),10 a standardized and validated instrument that has been used widely among cardiac populations.4,11,12 The PHQ-9 quantifies the frequency of depressive symptoms experienced in the past 2 weeks based on the 9 criteria for a major depressive disorder described in the Diagnostic and Statistical Manual of Mental Disorders (fourth edition; DSM).13 Each item is answered along a 4-point Likert scale with responses ranging from 0 (not at all) to 3 (nearly every day); a sum score between 0 and 27 points is derived by adding all responses. A PHQ-9 score ≥10 is commonly used as a screening criterion that has 88% sensitivity and specificity to detect a major depressive disorder.10 Depressive symptoms can further be classified according to severity: none (scores 0 to 4), mild (scores 5 to 9), moderate (scores 10 to 14), moderately severe (15 to 19), and severe (scores ≥20).
Depression and AMI in Young Patients  Smolderen et al

Disease-specific health status was assessed with the Seattle Angina Questionnaire (SAQ; physical limitations, angina frequency, and quality of life domains were analyzed) during the in-person interview at study enrollment. This instrument asks patients to reflect on the health status that they experienced in the 4 weeks prior to the assessment. This widely used instrument has been validated and used in a variety of coronary artery disease populations, including AMI.\textsuperscript{14–18} Scores on each subscale range from 0 to 100, with higher scores indicating better health status (i.e., fewer physical limitations, less angina, and better quality of life).

Generic health status at the time of patients’ AMI admission was measured with the visual analog scale of the standardized EuroQoL 5D instrument, which asks patients to rate their current health on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state).\textsuperscript{19,20}

Perceived stress levels that patients experienced over the past month were assessed with the 14-item Perceived Stress Scale (PSS).\textsuperscript{21} Items are answered along a 5-point Likert scale, and scores on this instrument range from 0 to 56, with higher scores referring to higher stress levels. The PSS has been used previously in AMI populations.\textsuperscript{22}

Sociodemographic factors considered in this study were age and self-identified race (black, white, other [used as reference category in our multivariable models]). For US patients, an additional ethnicity variable was included (Hispanic versus not). Ethnicity is a different variable than race, for example, patients can be Hispanic and black at the same time. Race and ethnicity categories were captured using the revised 1997 Office of Management and Budget definitions.\textsuperscript{23}

Socioeconomic status was quantified by defining patients’ marital status, highest education, working status, health insurance, and practice of avoiding health care because of cost. All of this information was obtained through patient interviews.

Medical history and clinical characteristics at AMI presentation were abstracted for prior coronary symptoms. Coronary disease included AMI, percutaneous coronary intervention or coronary artery bypass grafting, congestive heart failure, and angina. Other cardiac risk factors and comorbidities included hypertension, current smoking (within past 30 days), obesity (body mass index $\geq 30$ kg/m$^2$), prior stroke or transient ischemic attack, peripheral arterial disease, renal dysfunction, cancer, and chronic lung disease. Clinical severity of patients’ AMI presentations was assessed by Killip class, peak troponin level, hemodynamic instability, final AMI diagnosis (ST-elevation AMI), and ejection fraction <40%. Cardiac symptoms included typical versus atypical chest pain, back pain, abdominal pain, nausea, other pain, shortness of breath, fatigue, other cardiac symptoms, and other acute noncardiac conditions at arrival (e.g., stroke, acute kidney failure, sepsis), a variable previously shown to be highly prognostic of mortality.\textsuperscript{24} The number of cardiac symptoms experienced by a patient were counted and recorded as a continuous variable.

Finally, information about antidepressants at discharge and newly prescribed antidepressants was abstracted from patients’ medical records.

Study Sample

Of the 5585 patients meeting eligibility criteria, 3572 (64%) were enrolled (2985 from the United States, 516 from Spain, 71 from Australia). The most common reasons for not enrolling were refusal of informed consent and discharge occurring prior to contact by the site study coordinator. Because our primary objective was to look at the association between depressive symptoms and patient characteristics in women and men with an AMI, we restricted our depression analyses to those who had PHQ-9 scores available. Depressive symptom scores were uncommonly missing ($\leq 4\%$; n=148) without differences by sex (Table S3).

Statistical Analysis

To provide an overview of the patient characteristics for the overall sample and by sex, frequencies and percentages were used to summarize categorical variables, and medians, means, standard deviations, and interquartile ranges were reported to summarize continuous variables. Chi-square tests for categorical variables and Wilcoxon rank-sum tests for continuous variables were used to assess statistical significance. A $P$ value $<0.05$ was considered statistically significant. In addition, Cohen’s $d$ effect sizes were calculated for continuous variables for which mean and standard deviations were provided.\textsuperscript{25}

To describe the burden of depressive symptoms by sex, we used the same descriptive approach: We summarized data on the history of depression and current symptoms of depression for the overall sample and by sex. Similarly, we described the demographic, socioeconomic, and clinical profiles of patients with AMI by sex and depression status.

Next, logistic regression models were used to assess the independent relationship between sex and PHQ-9 scores $\geq 10$. Sociodemographic, socioeconomic, medical history, and health status variables were added sequentially to identify the association of sex with depressive symptoms. The first model included only sex; age and race were added next, and the third step included socioeconomic variables (marital status, education level, working status). The fourth step added medical history information, including congestive heart failure; prior AMI, percutaneous coronary intervention, or coronary artery bypass grafting; prior stroke or transient ischemic attack; peripheral arterial disease; history of
diabetes; final AMI diagnosis; smoking in the past 30 days; obesity; and chronic lung disease. In the final step, health status information was added (SAQ subscales for angina frequency, physical limitation, and quality of life). All analyses were performed using SAS 9.3 (SAS Institute Inc). Figures were created in R 2.15.1 (R Foundation for Statistical Computing).

Results

Patient Characteristics for the Overall Population and by Sex

There were 1175 men and 2397 women. Most characteristics were similar between men and women (Table 1); however, lower proportions of women were white and married. Women presented with higher rates of diabetes and obesity but had lower rates of hypercholesterolemia compared with men. Women had also had higher rates of cancer and chronic lung disease. Mean SAQ physical limitation scores in patients who recently had an AMI were lower in women compared with men (Cohen’s $d=0.33$). About half of patients reported angina symptoms in the 4 weeks leading up to their AMI, with lower SAQ angina frequency and SAQ quality of life scores in women compared with men (Cohen’s $d=0.20$ and 0.21, respectively). The same pattern was observed for generic health status (Cohen’s $d=0.19$). As compared with men, perceived stress levels were highest among women (Cohen’s $d=0.40$).

Depressive Symptoms by Sex

Significantly more women than men reported having had a diagnosis of depression in the past (48% versus 24%; $P<0.0001$). At the time of their AMI, more women than men had significant depressive symptoms (PHQ-9 scores $\geq 10$ in 39% of women versus 22% of men; $P<0.0001$). Of those who had a history of depression, more than twice as many women (26%) presented with PHQ-9 scores $\geq 10$ as men (10%; $P<0.0001$). Women also scored higher for the overall PHQ-9 (mean score of $9\pm7$ versus $6\pm6$ in men; Cohen’s $d=0.46$; $P<0.0001$) (Table 2). Women were more likely to have PHQ-9 scores $\geq 10$ in all 3 countries (Table S4).

Independent Association Between Sex and Depressive Symptoms

Women had 2.28 greater odds of presenting with depressive symptoms at the time of AMI compared with men (95% CI 1.94 to 2.69). After adjustment for demographic, socioeconomic, clinical, and health status variables, the association between female sex and significant depressive symptoms persisted (odds ratio 1.64; 95% CI 1.36 to 1.98) (Table 4). Other characteristics associated with having depressive symptoms included history of cardiac disease, nonmarried status, and being unemployed (Figure shows adjusted model results, and Table S5 shows the fully adjusted model). Sensitivity analyses were run to verify whether our findings were different if each participating country’s data were individually excluded to verify whether findings were robust across these international settings, and results remained essentially unchanged (data not shown).

Discussion

Although depression was recently recognized as a risk factor for adverse medical outcomes in patients with AMI, many basic questions remain with regard to the extent to which this risk factor is prevalent among younger patients with AMI. We found a much greater prevalence of prior depression and concurrent depressive symptoms among young women with...
Table 1. Patient Characteristics for the Overall Sample and by Sex

|                          | Overall (N=3572, 100%) | Men (n=1175, 32.9%) | Women (n=2397, 67.1%) |
|--------------------------|------------------------|---------------------|-----------------------|
|                          | n (%)                  | n (%)               | n (%)                 |
| Sociodemographic         |                        |                     |                       |
| characteristics          |                        |                     |                       |
| Age, range, y            | 18 to 55               | 23 to 55            | 18 to 55              |
| Age, median (IQR), y     | 48 (44 to 52)          | 48 (43 to 52)       | 48 (44 to 52)         |
| Race                     |                        |                     |                       |
| White                    | 2800 (78)              | 980 (84)            | 1820 (76)             |
| Black                    | 554 (16)               | 114 (10)            | 440 (18)              |
| Other                    | 212 (6)                | 79 (7)              | 133 (6)               |
| Hispanic                 | 269 (8)                | 92 (8)              | 177 (7)               |
| Married                  | 1827 (51)              | 678 (58)            | 1149 (48)             |
| Socioeconomic            |                        |                     |                       |
| characteristics          |                        |                     |                       |
| Education                |                        |                     |                       |
| Less than high school    | 185 (5)                | 47 (4)              | 138 (6)               |
| High school              | 1459 (42)              | 489 (43)            | 970 (41)              |
| More than high school    | 1860 (53)              | 612 (53)            | 1248 (53)             |
| Work full or part time   | 2204 (62)              | 856 (73)            | 1348 (57)             |
| Health insurance         | 2870 (80)              | 920 (78)            | 1950 (81)             |
| Avoid getting health care | 1070 (30)              | 333 (28)            | 737 (31)              |
| because of cost          |                        |                     |                       |
| Medical history          |                        |                     |                       |
| Prior AMI, PCI, or CABG  | 682 (19)               | 241 (21)            | 441 (18)              |
| Angina                   | 966 (27)               | 307 (26)            | 659 (28)              |
| Congestive heart failure | 141 (4)                | 24 (2)              | 117 (5)               |
| Hypertension             | 2260 (63)              | 730 (62)            | 1530 (64)             |
| Diabetes                 | 1246 (35)              | 317 (27)            | 929 (39)              |
| Hypercholesterolemia     | 3062 (86)              | 1080 (92)           | 1982 (83)             |
| Smoked within past 30 days | 2133 (60)             | 697 (59)            | 1436 (60)             |
| Obesity (BMI >=30 kg/m²) | 1745 (49)              | 524 (45)            | 1221 (51)             |
| Prior stroke/TIA         | 147 (4)                | 27 (2)              | 120 (5)               |
| Peripheral arterial disease | 80 (2)                | 23 (2)              | 57 (2)                |
| Renal dysfunction        | 367 (10)               | 91 (8)              | 276 (12)              |
| Cancer                   | 119 (3)                | 23 (2)              | 96 (4)                |
| Chronic lung disease     | 363 (10)               | 65 (6)              | 298 (12)              |
| Health status            |                        |                     |                       |
| SAQ physical limitation score, mean (SD) | 81 (25) | 87 (21) | 79 (27) |
| SAQ angina frequency score, mean (SD) | 84 (20) | 87 (18) | 83 (21) |
| SAQ angina frequency categories |                      |                     |                       |
| Daily (0 to 30)          | 96 (3)                 | 16 (1)              | 80 (3)                |
| Weekly (31 to 60)        | 566 (16)               | 158 (14)            | 408 (17)              |
| Monthly (61 to 99)       | 1235 (35)              | 414 (35)            | 821 (34)              |
| None (100)               | 1656 (46)              | 583 (50)            | 1073 (45)             |
| SAQ quality of life score, mean (SD) | 57 (24) | 60 (22) | 55 (25) |
Table 1. Continued

|                                | Overall (N=3572, 100%) | Men (n=1175, 32.9%) | Women (n=2397, 67.1%) |
|--------------------------------|------------------------|---------------------|------------------------|
|                                | n (%)                  | n (%)               | n (%)                  |
| EuroQoL 5D VAS, mean (SD)      | 64 (22)                | 67 (20)             | 63 (22)                |
| PSS-14, mean (SD)              | 26 (10)                | 23 (10)             | 27 (10)                |

Clinical characteristics at AMI presentation

Killip class

|                                | Overall (N=3572, 100%) | Men (n=1175, 32.9%) | Women (n=2397, 67.1%) |
|--------------------------------|------------------------|---------------------|------------------------|
|                                | n (%)                  | n (%)               | n (%)                  |
| I, no heart failure            | 3242 (92)              | 1083 (93)           | 2159 (91)              |
| II, heart failure              | 110 (3)                | 26 (2)              | 84 (4)                 |
| III, pulmonary edema           | 26 (1)                 | 4 (1)               | 22 (1)                 |
| IV, cardiogenic shock          | 21 (1)                 | 5 (1)               | 16 (1)                 |
| Peak troponin level, median (IQR), ng/mL | 6.9 (1.5 to 28.0)      | 9.6 (2.0 to 37.5)   | 5.8 (1.4 to 23.1)     |
| Hemodynamic instability        | 309 (9)                | 97 (8)              | 212 (9)                |
| Final AMI diagnosis: STEMI      | 1860 (52)              | 705 (60)            | 1155 (48)              |
| Ejection fraction <40%         | 370 (11)               | 127 (11)            | 243 (11)               |
| Experienced typical chest pain | 2835 (79)              | 980 (83)            | 1855 (77)              |
| Experienced atypical chest pain| 634 (18)               | 164 (14)            | 470 (20)               |
| Experienced back pain          | 514 (14)               | 118 (10)            | 396 (17)               |
| Experienced abdominal pain     | 158 (4)                | 42 (4)              | 116 (5)                |
| Experienced nausea             | 1477 (41)              | 409 (35)            | 1068 (45)              |
| Experienced other type of pain | 729 (20)               | 237 (20)            | 492 (21)               |
| Experienced shortness of breath| 1577 (44)              | 512 (44)            | 1065 (44)              |
| Experienced fatigue            | 387 (11)               | 116 (10)            | 271 (11)               |
| Experienced other symptoms     | 2284 (64)              | 739 (63)            | 1545 (64)              |
| Had other acute noncardiac conditions at arrival | 173 (5)               | 41 (4)              | 132 (6)                |
| Number of symptoms, median (IQR) | 3 (2 to 4)            | 3 (2 to 4)          | 3 (2 to 4)             |

AMI indicates acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; IQR, interquartile range; PCI, percutaneous coronary intervention; PSS-14, 14-item Perceived Stress Scale; SAQ, Seattle Angina Questionnaire; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack; VAS, visual analog scale.

Table 2. Descriptive Overview of Comorbid Depression Rates (History and Current Symptoms) for the Overall Sample and by Sex

|                                | Overall (N=3572, 100%) | Men (n=1175, 32.9%) | Women (n=2397, 67.1%) |
|--------------------------------|------------------------|---------------------|------------------------|
|                                | n (%)                  | n (%)               | n (%)                  |
| History of depression          | 1421 (40)              | 280 (24)            | 1141 (48)              |
| PHQ-9 overall score, mean (SD)*| 8 (6)                  | 6 (6)               | 9 (7)                  |
| PHQ-9 ≥10                      | 1131 (33)              | 245 (22)            | 886 (39)               |

PHQ-9 depression levels

|                                | Overall (N=3572, 100%) | Men (n=1175, 32.9%) | Women (n=2397, 67.1%) |
|--------------------------------|------------------------|---------------------|------------------------|
|                                | n (%)                  | n (%)               | n (%)                  |
| No depression (score 0 to 4)    | 1333 (39)              | 577 (51)            | 756 (33)               |
| Mild depression (score 5 to 9)  | 960 (28)               | 310 (27)            | 650 (28)               |
| Moderate depression (score 10 to 14) | 552 (16)           | 141 (12)            | 411 (18)               |
| Moderately severe depression (score 15 to 19) | 364 (11)         | 68 (6)              | 296 (13)               |
| Severe depression (score ≥20)   | 215 (6)                | 36 (3)              | 179 (8)                |
| PHQ-9 ≥10 and history of depression | 710 (21)            | 114 (10)            | 596 (26)               |

PHQ-9 indicates 9-item Patient Heath Questionnaire.
*Only 3424 subjects had PHQ-9 overall scores (n=1132 for men, and n=2292 for women).
Table 3. Descriptive Overview of Patient Characteristics Presented by Sex and Depression Status (PHQ-9 <10 PHQ-9 ≥10)

| Characteristic                           | Men PHQ-9 <10 n=887, 78.4% | Men PHQ-9 ≥10 n=245, 21.6% | P value | Women PHQ-9 <10 n=1406, 61.3% | Women PHQ-9 ≥10 n=886, 38.7% | P value |
|------------------------------------------|----------------------------|-----------------------------|---------|-------------------------------|-------------------------------|---------|
| Sociodemographic characteristics        |                            |                             |         |                               |                               |         |
| Age, median (IQR), years                 | 48 (43 to 52)              | 48 (44 to 51)               | 0.76    | 48 (44 to 52)                 | 48 (44 to 52)                 | 0.52    |
| Race                                     |                            |                             | 0.61    |                               |                               | 0.06    |
| White                                    | 736 (83)                   | 209 (85)                    |         | 1056 (75)                     | 694 (79)                      |         |
| Black                                    | 87 (10)                    | 23 (10)                     |         | 261 (19)                      | 153 (17)                      |         |
| Other                                    | 62 (7)                     | 13 (5)                      |         | 88 (6)                        | 37 (4)                        |         |
| Hispanic                                 | 57 (6)                     | 31 (13)                     | 0.012   | 106 (8)                       | 62 (7)                        | 0.55    |
| Married                                  | 536 (61)                   | 118 (48)                    | 0.0005  | 721 (51)                      | 374 (42)                      | <0.0001 |
| Education                                |                            |                             | 0.0013  |                               |                               | 0.0021  |
| Less than high school                    | 34 (4)                     | 10 (4)                      |         | 76 (5)                        | 56 (6)                        |         |
| High school                              | 342 (39)                   | 126 (52)                    |         | 532 (38)                      | 392 (45)                      |         |
| More than high school                    | 491 (57)                   | 105 (44)                    |         | 778 (56)                      | 423 (49)                      |         |
| Work full or part time                   | 685 (78)                   | 144 (59)                    | <0.0001 | 901 (64)                      | 394 (45)                      | <0.0001 |
| Health insurance                         | 724 (82)                   | 171 (70)                    | <0.0001 | 1176 (84)                     | 689 (78)                      | 0.0003  |
| Avoid getting health care because of cost| 210 (24)                   | 107 (44)                    | <0.0001 | 349 (25)                      | 361 (41)                      | <0.0001 |
| Medical history                          |                            |                             |         |                               |                               |         |
| Prior AMI, PCI, or CABG                  | 166 (19)                   | 68 (28)                     | 0.0020  | 234 (17)                      | 189 (21)                      | 0.0051  |
| Congestive heart failure                 | 10 (1)                     | 12 (5)                      | 0.0022  | 57 (4)                        | 58 (7)                        | 0.0078  |
| Hypertension                             | 529 (60)                   | 176 (72)                    | 0.0005  | 836 (59)                      | 624 (70)                      | <0.0001 |
| Diabetes                                 | 211 (24)                   | 95 (39)                     | <0.0001 | 492 (35)                      | 394 (44)                      | <0.0001 |
| Hypercholesterolemia                     | 805 (91)                   | 235 (96)                    | 0.0088  | 1131 (80)                     | 759 (86)                      | 0.0014  |
| Smoked within past 30 days               | 493 (56)                   | 176 (72)                    | <0.0001 | 762 (54)                      | 603 (68)                      | <0.0001 |
| Obesity (BMI ≥30 kg/m²)                  | 384 (43)                   | 121 (49)                    | 0.0920  | 667 (48)                      | 492 (56)                      | 0.0002  |
| Prior stroke/TIA                         | 17 (2)                     | 10 (4)                      | 0.0497  | 65 (5)                        | 48 (5)                        | 0.39    |
| Peripheral arterial disease              | 13 (1)                     | 8 (3)                       | 0.0670  | 31 (2)                        | 25 (3)                        | 0.36    |
| Renal dysfunction                        | 69 (8)                     | 19 (8)                      | 0.9945  | 148 (11)                      | 114 (13)                      | 0.08    |
| Cancer                                   | 16 (2)                     | 7 (3)                       | 0.3009  | 54 (4)                        | 37 (4)                        | 0.69    |
| Chronic lung disease                     | 40 (5)                     | 21 (9)                      | 0.0128  | 116 (8)                       | 170 (19)                      | <0.0001 |
| Health status                            |                            |                             |         |                               |                               |         |
| SAQ physical limitation score, mean (SD) | 91 (17)                    | 74 (26)                     | <0.0001 | 86 (22)                       | 67 (31)                       | <0.0001 |
| SAQ quality of life score, mean (SD)     | 63 (21)                    | 50 (22)                     | <0.0001 | 61 (23)                       | 45 (25)                       | <0.0001 |
| PSS-14, mean (SD)                        | 21 (8)                     | 32 (8)                      | <0.0001 | 23 (8)                        | 34 (8)                        | <0.0001 |
| Clinical characteristics at presentation |                            |                             |         |                               |                               |         |
| Killip class                             |                            |                             | 0.0173  |                               |                               | 0.37    |
| I, no heart failure                      | 825 (94)                   | 217 (89)                    |         | 1273 (92)                     | 793 (91)                      |         |
| II, heart failure                        | 14 (2)                     | 12 (5)                      |         | 42 (3)                        | 38 (4)                        |         |
| III, pulmonary edema                     | 2 (1)                      | 2 (1)                       |         | 13 (1)                        | 9 (1)                         |         |
| IV, cardiogenic shock                    | 4 (1)                      | 1 (1)                       |         | 7 (1)                         | 8 (1)                         |         |

Continued
AMI than among young men. Even after adjusting for numerous sociodemographic, clinical, and disease severity characteristics, young women with AMI had 60% greater odds of having significant depressive symptoms than young men. Moreover, at the time of their AMI, women with a history of clinical depression were particularly vulnerable to experiencing depressive symptoms compared with men with a history of depression; up to a quarter of women with a history of depression had current depressive symptoms versus 10% of men with a history of depression. Although there is literature documenting sex differences in depression and cardiovascular disease, the finding of higher prevalence of depressive symptoms in young women with AMI compared with men, in particular, has important implications.

Although preliminary studies have shed important insight in this area, young women were often underrepresented in prior studies of patients with AMI, and the studies are old or missed detailed patient and depression information.1,4,5,8,26 The VIRGO study was able to accommodate these shortcomings and added new insights into the extent of patients’

**Table 3.** Continued

|                          | Men PHQ-9 <10 n=887, 78.4% | PHQ-9 ≥10 n=245, 21.6% | P value | Women PHQ-9 <10 n=1406, 61.3% | PHQ-9 ≥10 n=886, 38.7% | P value |
|--------------------------|-----------------------------|------------------------|---------|-----------------------------|------------------------|---------|
| Final AMI diagnosis: STEMI| 542 (61)                    | 138 (56)               | 0.1764  | 697 (50)                    | 408 (46)               | 0.1002  |
| Experienced typical chest pain | 745 (84)                  | 195 (80)               | 0.1043  | 1098 (78)                   | 677 (76)               | 0.3478  |
| Experienced atypical chest pain | 115 (13)                  | 46 (19)                | 0.0212  | 260 (18)                    | 186 (21)               | 0.1408  |
| Experienced back pain    | 91 (10)                     | 22 (9)                 | 0.5542  | 231 (16)                    | 154 (17)               | 0.5528  |
| Experienced abdominal pain | 26 (3)                      | 15 (6)                 | 0.0180  | 64 (5)                      | 47 (5)                 | 0.4136  |
| Experienced nausea       | 298 (34)                    | 94 (38)                | 0.1647  | 620 (44)                    | 409 (46)               | 0.3329  |
| Experienced other type of pain | 165 (19)                   | 59 (24)                | 0.0567  | 290 (21)                    | 177 (20)               | 0.7074  |
| Experienced shortness of breath | 364 (41)                  | 130 (53)               | 0.0008  | 565 (40)                    | 452 (51)               | <0.0001 |
| Experienced fatigue      | 80 (9)                      | 33 (13)                | 0.0397  | 141 (10)                    | 117 (13)               | 0.0191  |
| Experienced other symptoms | 544 (61)                    | 164 (67)               | 0.1084  | 904 (64)                    | 575 (65)               | 0.7691  |
| Had other acute noncardiac conditions at arrival | 23 (3)                      | 17 (7)                 | 0.0012  | 65 (5)                      | 55 (6)                 | 0.1099  |
| Number of symptoms, median (IQR) | 3 (2, 4)                   | 3 (2, 4)               | 0.0004  | 3 (2, 4)                    | 3 (2, 4)               | 0.0035  |

**Depression treatment information during AMI admission**

|                          |                     |                       |         |                     |                       |         |
|--------------------------|---------------------|-----------------------|---------|---------------------|-----------------------|---------|
| Antidepressant use at discharge | 60 (7)          | 47 (19)               | <0.0001 | 217 (15)            | 274 (31)              | <0.0001 |
| Newly prescribed antidepressants | 15 (2)          | 6 (3)                 | 0.29    | 25 (2)              | 44 (7)                | <0.0001 |

**Table 4.** Sequential Logistic Regression Results for the Relationship Between Female Sex and PHQ-9 Scores ≥10

| Model Number | Odds Ratio for Female Sex (95% CI) | Covariates Included in the Model |
|--------------|-------------------------------------|----------------------------------|
| 1            | 2.28 (1.94 to 2.69)                 | Sex                              |
| 2            | 2.30 (1.95 to 2.71)                 | Sex, age, race                    |
| 3            | 1.99 (1.68 to 2.36)                 | Sex, age, race, marital status, education level, employment status |
| 4            | 1.86 (1.56 to 2.22)                 | Sex, age, race, marital status, education level, employment status, congestive heart failure, prior AMI/PCI/CABG, prior stroke/TIA, peripheral arterial disease, history of diabetes, STEMI, smoking in past 30 days, obesity status, chronic lung disease |
| 5            | 1.64 (1.36 to 1.98)                 | Sex, age, race, marital status, education level, employment status, congestive heart failure, prior AMI/PCI/CABG, prior stroke/TIA, peripheral arterial disease, history of diabetes, STEMI, smoking in past 30 days, obesity status, chronic lung disease, SAQ physical limitation, SAQ quality of life |

AMI indicates acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; IQR, interquartile range; PCI, percutaneous coronary intervention; PHQ, 9-item Patient Health Questionnaire; PSS-14, 14-item Perceived Stress Scale; SAQ, Seattle Angina Questionnaire; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack.
Depressive symptomatology. This understanding may be helpful in future studies examining depression as a potential explanatory mechanism for the adverse outcomes of younger women recovering from an AMI. Importantly, a novel finding of this study, the long lifetime history of depression with greater depressive symptoms at the time of an AMI, suggests inadequate treatment of known depression and warrants further investigation into biological (eg, genetic, inflammation) and psychosocial triggers that may underlie this unusually high depression burden among young women. An alternative explanation for the increased depressive symptom burden may be that women with depression suffered from a high comorbidity burden (eg, diabetes, obesity, chronic lung disease). This burden may predispose women to experiencing more depressive symptoms, although adjustment for these factors did not affect the association between female sex and having increased depressive symptoms in the current study.

Regardless of cause, having depressive symptoms that interfere with daily functioning warrants appropriate treatment in its own right. Experiencing depressive symptoms and also having coronary disease may further complicate recovery because both limit daily function and may negatively affect patients’ rehabilitation.27 Another reason why depressive symptoms in cardiac patients deserve special consideration is that prevalence seems to be disproportionately high, and this remains the case over the years. Both in women and men with AMI who were aged 18 to 55 years, 3 times as many patients had PHQ-9 scores ≥10 compared with the general population (depression rates among men and women aged 40 to 59 years are 7% and 12%, respectively, as measured in the US National Health and Nutrition Examination Survey study with the PHQ-9 ≥10 criterion).29 The prevalence estimates for depression in the younger patients with AMI in this study are also fairly consistent with those obtained from data collected 5 to 8 years ago. In the PREMIER study, 40% of women aged <60 years had PHQ-9 scores ≥10 and 22% of younger men had increased PHQ-9 scores, suggesting that little progress has been made to effectively address this burden.4 Despite several initiatives to better recognize and treat depression in coronary artery disease and the knowledge that depression...
constitutes a major risk for future adverse AMI prognosis,\(^5,6\) prevalence rates for depression remain exceedingly high.

A study finding that requires further reflection is that nearly half of younger women (≤55 years) had a diagnosis of depression at some point in their lives versus 24% of younger men (≤55 years); however, half of those who had PHQ-9 scores ≥10 around the time of their AMI did not have a history of depression. The same pattern was observed for younger men, except that their depression history rates were half those of younger women. Although our cross-sectional design and the self-report of lifetime history of depression may limit us in finding an actual explanation for our findings, several hypotheses can be formulated and will need further testing in the future. Patients’ new depressive symptoms may have been specifically associated with the impending AMI or perhaps, in a substantial amount of patients, depressive symptoms went unnoticed and untreated in the past. It is known that women who present with chest pain at the emergency department without evidence of coronary disease but with cardiac risk factors already seem vulnerable to experiencing high rates of depressive symptoms.\(^9\) The tenacity of women’s depressive symptom burden in cardiac disease requires more extensive evaluation to understand whether patients’ symptoms of depression were correctly diagnosed or adequately treated in the past, whether other psychological comorbidities are present that need to be addressed along with the depression, whether the depression had been completely in remission in the past, or whether women tend to experience more treatment-resistant symptoms of depression. Another potential explanation may be that the very high rate of depressive symptoms is, in part, secondary to the experience of the AMI. Regardless, depression seems to be a recurrent concern over the course of life in a large group of patients with AMI.

Increased awareness and intensified treatment for coronary patients’ depressive symptoms can be very beneficial. Similarly, the high stress scores noted in both younger men and women who had PHQ-9 scores ≥10 are modifiable and important treatment targets that are also associated with adverse cardiac disease outcomes.\(^22,33\) Recently, several intervention studies have been shown to be helpful in reducing depressive symptoms and stress, improving patients’ quality of life, and rendering promising results with regard to patients’ cardiovascular prognosis.\(^30,31,34\) These intervention studies combined elements of cognitive–behavioral and problem-solving therapies, stress-reduction techniques, and stepped depression and collaborative care programs. The profile information provided in this study could be used to design a tailored prevention or intervention program incorporating these techniques. Through existing community programs that have already identified younger persons with vulnerable socioeconomic positions (eg, not having a partner, being unemployed, having less education), one could focus on preventive strategies and improving recognition of depression and on aggressive management of cardiovascular risk factors. The current study highlights that in such programs, potentially lower literacy levels and other socioeconomic barriers need to be considered because younger patients with depressive symptoms presented with very unfavorable socioeconomic profiles. Having this specific information about this younger population facing depression is important for designing targeted depression-intervention programs. The correlates of depression seem to be unique to the challenges of the phase of life that each individual faces. As a comparison, at older ages, female sex is still a predictor of having depression, but other factors like functional and cognitive decline and social isolation seem to be more prominent characteristics of persons dealing with depressive symptoms.\(^35\) Providing access to tailor-made programs that address the risk factors unique to a younger population like that studied in VIRGO and using some of the elements studied in recent depression-intervention studies could offer a way to attenuate the high coronary and psychiatric risk of these younger persons.

This study should be interpreted within the context of several potential limitations. It is impossible to discern whether the depressive symptoms noted in this observational study were a cause or an effect of patients’ AMI, although the PHQ-9 inquires about symptoms over the past 2 weeks (prior to the AMI), and women’s increased risk of depression was independent of AMI severity, comorbid conditions, cardiovascular risk factors, and health status. Regardless of the direction of the relationship, it is important to note that depressive symptoms can be treated successfully. There is a potential concern about recall bias associated with the self-report data on lifetime history of depression; however, previous research has indicated that this way of measuring lifetime history of depression may result in underreporting of lifetime history of depression rates; if anything, the estimates of the depressive symptom burden in our AMI population may reflect underrepresentation.\(^36,37\) Other limitations of this study include the potential for residual confounding, the lack of a diagnostic interview for a DSM diagnosis of current depression,\(^33\) and the inability to look at potential mechanisms as to why women incurred the highest risk of experiencing depressive symptoms prior to their AMI. Hormonal differences, combining several life roles, being a single parent, and working in lower paid jobs are just a few potential reasons identified in the past that could help explain the observed sex differences in depressive symptoms.\(^38\) Future studies will be needed to replicate our findings and to better define the mechanisms of young patients’ depressive symptoms.
In summary, the burden of depressive symptoms is very high among young patients with an AMI, particularly among younger women. Regardless of sex, depressive symptoms seem to primarily strike patients with lower socioeconomic status and are accompanied by high levels of stress and decreased functional status. This information will be useful to target future prevention and intervention programs that can help address depression as an important cardiac risk factor in this vulnerable group of patients.

Sources of Funding

VIRGO was supported by grant R01 HL08 1153-01A1K from the National Heart, Lung, Blood Institute, Department of Health and Human Services. IMJOVEN was supported in Spain by PI 081614 from the Fondo de Investigaciones Sanitarias del Instituto Carlos III, Ministry of Science and Technology, and additional funds from the Centro Nacional de Investigaciones Cardiovasculares. Dr Smolderen was supported by the Netherlands Organization for Scientific Research (VENI-916.11.179) and by PCORI (1 IP2 PI00753-01; CE-1304-6677).

Disclosures

Dr Bueno was supported in part by grant BA08/90010 from the Fondo de Investigación Sanitaria del Instituto de Salud Carlos III, Spain and has received advisory/consulting fees from AstraZeneca, Bayer, Daichii-Sankyo, Eli-Lilly, Menarini, Novartis, Sanofi and Servier and research grants from AstraZeneca.

References

1. Vaccarino V, Krumholz HM, Yarzebski J, Gore JM, Goldberg RJ. Sex differences in 2-year mortality after hospital discharge for myocardial infarction. Ann Intern Med. 2001;134:173–181.
2. Vaccarino V, Parsons L, Every NR, Baron HV, Krumholz HM. Sex-based differences in early mortality after myocardial infarction. National registry of myocardial infarction 2 participants. N Engl J Med. 1999;341:217–225.
3. Thombs BD, Bass EB, Ford DE, Stewart KJ, Tsilidis KK, Patel U, Fauerbach JA, Bush DE, Ziegelstein RC. Prevalence of depression in survivors of acute myocardial infarction. J Gen Intern Med. 2006;21:30–38.
4. Mallik S, Spertus JA, Reid KJ, Krumholz HM, Rumsfeld JS, Weintraub WS, Agarwal P, Santra M, Bidyasar S, Lichtman JH, Wenger NK, Vaccarino V. Depressive symptoms after acute myocardial infarction: evidence for highest rates in younger women. Arch Intern Med. 2006;166:876–883.
5. Frasure-Smith N, Lesperance F, Talajic M. Depression and 18-month prognosis after myocardial infarction. Circulation. 1995;91:999–1005.
6. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, Freedland KE, Jaffe AS, Leibheit-Limon EC, Sheps DS, Vaccarino V, Wulsin L, on behalf of the American Heart Association Statistics Committee of the Council on Epidemiology and Prevention and the Council on Cardiovascular and Stroke Nursing. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American heart association. Circulation. 2014;129:1350–1369.
7. Hare DL, Toukhstai SR, Johansson P, Jaarsma T. Depression and cardiovascular disease: a clinical review. Eur Heart J. 2014;35:1365–1372.
8. Parasur R, Rumsfeld JS, Reid KJ, Buchan D, Dawood N, Khizer S, Lichtman J, Vaccarino V. Impact of depression on sex differences in outcome after myocardial infarction. Circ Cardiovasc Qual Outcomes. 2009;2:33–40.
9. Lichtman JH, Lorenze NP, D’Onofrio G, Spertus JA, Lindau ST, Morgan TM, Herrin J, Bueno H, Mattarya J, Rider PM, Krumholz HM. Variation in recovery: role of gender on outcomes of young ami patients (virgo) study design. Circ Cardiovasc Qual Outcomes. 2010;3:684–693.
10. Kroeneke K, Spitzer RL. The phq-9: a new depression diagnostic and severity measure. Psychiatr Ann. 2002;32:509–521.
11. Ruo B, Rumsfeld JS, Hlatky MA, Liu H, Brower WS, Whooley MA. Depressive symptoms and health-related quality of life: the heart and soul study. JAMA. 2003;290:215–221.
12. Whooley MA, de Jonge P, Vittinghoff E, Otte C, Moors R, Carney RM, Ali S, Dowray S, Na B, Feldman MD, Schiller NB, Brower WS. Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease. JAMA. 2008;300:2379–2388.
13. American psychiatric association. Diagnostic and statistical manual of mental disorders, fourth edition (dsm-iv). Washington, DC: American Psychiatric Publishing; 1994.
14. Mozaffarian D, Bryson CL, Spertus JA, McDonell MB, Fihn SD. Anginal symptoms consistently predict total mortality among outpatients with coronary artery disease. Am Heart J. 2003;146:1015–1022.
15. Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonell M, Fihn SD. Development and evaluation of the seattle angina questionnaire: a new functional status measure for coronary artery disease. J Am Coll Cardiol. 1995;25:333–341.
16. Spertus JA, Jones P, McDonell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. Circulation. 2002;106:43–49.
17. Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Fihn SD. Monitoring the quality of life in patients with coronary artery disease. Am J Cardiol. 1994;74:1240–1244.
18. Arnold SV, Morrow DA, Lei Y, Cohen DJ, Mahoney EM, Braunwald E, Chan PS. Economic impact of angina after an acute coronary syndrome: insights from the merlin-tim36 trial. Circ Cardiovasc Qual Outcomes. 2009;2:344–353.
19. Brooks R. Euroqol: the current state of play. Health Policy. 1994;6:53–72.
20. Euroqol G. Euroqol—a new facility for the measurement of health-related quality of life. Health Policy. 1990;16:199–208.
21. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24:385–396.
22. Arnold SV, Smolderen KG, Buchanan DM, Li Y, Spertus J. Perceived stress in myocardial infarction: long-term mortality and health status outcomes. J Am Coll Cardiol. 2012;60:1756–1763.
23. Recommendations from the interagency committee for the review of racial and ethnic standards to the of management and budget concerning changes to the standards for the classification of federal data on race and ethnicity. 2010. Centers for Disease Control and Prevention NCfHS. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6051a7.htm. Accessed March 11, 2015.
24. Lichtman JH, Spertus JA, Reid KJ, Radford MJ, Rumsfeld JS, Allen NB, Masoudi FA, Weintraub WS, Krumholz HM. Acute noncardiac conditions and in-hospital mortality in patients with acute myocardial infarction. Circulation. 2007;116:1925–1930.
25. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale, NJ: Erlbaum; 1988.
26. Frasure-Smith N, Lesperance F, Juneau M, Talajic M, Bourassa MG, Gender, depression, and one-year prognosis after myocardial infarction. Psychosom Med. 1999;61:26–37.
27. Dodson JA, Arnold SV, Reid KJ, Gill TM, Rich MW, Masoudi FA, Spertus JA, Krumholz HM, Alexander KP. Physical function and independence 1 year after myocardial infarction: observations from the translational research investigating underlying disparities in recovery from acute myocardial infarction: patients’ health status registry. Am Heart J. 2012;163:790–796.
28. Centers for Disease Control and Prevention NCHS. Quickstats: Prevalence of current depression* among persons aged ≥12 years, by age group and sex—United States, National Health and Nutrition Examination Survey, 2007–2010. National Health and Nutrition Examination Survey, 2007–2010. Centers for Disease Control and Prevention NCHS. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6051a7.htm. Accessed March 11, 2015.
29. Spitzer RL, Kroeneke K, Williams JB. Validation and utility of a self-report version of prime-md: the phq primary care study. Primary care evaluation of mental disorders. Patient health questionnaire, JAMA. 1999;282:1737–1744.
30. Davidson KW, Bigger JT, Burg MM, Carney RM, Chaplin WF, Czajkowski S, Gonnella J, Jafie AS,
Ladapo JA, Lesperance F, Medina V, Newman JD, Osorio GA, Parsons F, Schwartz JE, Shaffer JA, Shapiro PA, Sheps DS, Vaccarino V, Whang W, Ye S. Centralized, stepped, patient preference-based treatment for patients with post-acute coronary syndrome depression: codiacs vanguard randomized controlled trial. JAMA Intern Med. 2013;173:997–1004.

31. Rollman BL, Belnap BH, LeMenager MS, Mazumdar S, Houck PR, Counihan PJ, Kapoor WN, Schulberg HC, Reynolds CF II. Telephone-delivered collaborative care for treating post-cabg depression: a randomized controlled trial. JAMA. 2009;302:2095–2103.

32. Safdar B, Foody JM, D’Onofrio G. Depression as modifiable coronary risk factor in the emergency department chest pain observation unit: a pilot. Crit Pathw Cardiol. 2010;9:82–87.

33. Mommersteeg PM, Denollet J, Spertus JA, Pedersen SS. Health status as a risk factor in cardiovascular disease: a systematic review of current evidence. Am Heart J. 2009;157:208–218.

34. Orth-Gomer K, Schneiderman N, Wang HX, Walldin C, Blom M, Jernberg T. Stress reduction prolongs life in women with coronary disease: the stockholm women’s intervention trial for coronary heart disease (switchd). Circ Cardiovasc Qual Outcomes. 2009;2:25–32.

35. Djernes JK. Prevalence and predictors of depression in populations of elderly: a review. Acta Psychiatr Scand. 2006;113:372–387.

36. Patten SB. Recall bias and major depression lifetime prevalence. Soc Psychiatry Psychiatr Epidemiol. 2003;38:290–296.

37. Kruyslaar ME, Barendregt J, Vos T, de Graaf R, Spijker J, Andrews G. Lifetime prevalence estimates of major depression: an indirect estimation method and a quantification of recall bias. Eur J Epidemiol. 2005;20:103–111.

38. Kessler RC. Epidemiology of women and depression. J Affect Disord. 2003;74:5–13.
**SUPPLEMENTAL MATERIAL**

**Table S1 – Reasons For Not Enrolling Into the Study.** Categories are not mutually exclusive, as patients could have selected more than one reason for not participating into the study.*

| Reason                                         | N (%) |
|------------------------------------------------|-------|
| Discharged prior to being contacted by site study coordinator | 551 (29) |
| Refused informed consent                        | 949 (50) |
| Other reason                                    | 392 (21) |
| Spanish speaking and translator not available   | 11 (<1)  |

*202 patients had not had a recorded reason for not enrolling.

**Table S2 – Overview of Descriptives for Time Windows Around Patient Interviews.**

Baseline Interview Window (N=3,572)

| N (%)                   |
|-------------------------|
| Interviewed in-hospital | 3,280 (92%) |
| Interviewed 3 days of discharge | 292 (8%) |

**Table S3 – Missingness on PHQ-9 Score Overall and by Gender.**

| Overall (n=3,572) | Men (n=1,175) | Women (n=2,397) |
|-------------------|---------------|-----------------|
| Missing PHQ-9 score | 148 (4%) | 43 (4%) | 105 (4%) |
Table S4 – Depressive Symptoms (PHQ-9≥10) by Country and by Gender.

|                | Overall | Men  | Women |
|----------------|---------|------|-------|
| United States  | 34%     | 22%  | 39%   |
| Spain          | 31%     | 17%  | 38%   |
| Australia      | 25%     | 22%  | 27%   |
Table S5 - Fully Adjusted Logistic Regression Model Results Evaluating the Relationship Between Female Gender and PHQ-9 Scores ≥ 10. Odds Ratios [OR] and 95% Confidence Intervals [95% CI] are depicted. Abbreviations: PHQ-9, Patient Health Questionnaire-9 item version; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; HF, heart failure; TIA, transient ischemic attack; PAD, peripheral arterial disease; SAQ, Seattle Angina Questionnaire; STEMI, ST-elevation myocardial infarction.

| Variable                             | Odds Ratio | 95% CI     | P-Value |
|--------------------------------------|------------|------------|---------|
| **Socio-Demographic Characteristics** |            |            |         |
| Female gender                        | 1.67       | 1.38-2.01  | <0.0001 |
| Age (per 1 unit increase)            | 1.00       | 0.99-1.01  | 0.9866  |
| White race                           | 1.39       | 0.95-2.04  | 0.0009  |
| Black race                           | 0.87       | 0.57-1.34  | 0.0445  |
| **Socio-Economic Characteristics**   |            |            |         |
| Not married                          | 1.23       | 1.04-1.46  | 0.0177  |
| Less than high school education      | 1.16       | 0.81 – 1.67| 0.5796  |
| Completed some high school education | 1.10       | 0.93-1.32  | 0.8336  |
| Not Employed                         | 1.46       | 1.22-1.75  | <0.0001 |
| **Medical History**                  |            |            |         |
| Prior MI/PCI/CABG                    | 0.78       | 0.63-0.98  | 0.0305  |
| History of HF                        | 0.88       | 0.57-1.35  | 0.5474  |
| History of diabetes                  | 1.34       | 1.12-1.61  | 0.0013  |
| Smoked within past 30 days           | 1.67       | 1.40-2.00  | <0.0001 |
| Obese                                | 1.12       | 0.94-1.33  | 0.2043  |
| Prior stroke/TIA                     | 0.91       | 0.59-1.38  | 0.6453  |
| History of PAD                       | 0.78       | 0.46-1.35  | 0.3775  |
| History of lung disease              | 1.44       | 1.10-1.89  | 0.0076  |
| **Health Status**                    |            |            |         |
| SAQ physical limitations (per 1 unit increase) | 0.98 | 0.97-0.99 | <0.0001 |
| SAQ quality of life (per 1 unit increase)  | 0.98 | 0.97-0.98 | <0.0001 |
| STEMI diagnosis                      | 0.95       | 0.80-1.12  | 0.5434  |
Depressive Symptoms in Younger Women and Men With Acute Myocardial Infarction: Insights From the VIRGO Study

Kim G. Smolderen, Kelly M. Strait, Rachel P. Dreyer, Gail D’Onofrio, Shengfan Zhou, Judith H. Lichtman, Mary Geda, Héctor Bueno, John Beltrame, Basmah Safdar, Harlan M. Krumholz and John A. Spertus

*J Am Heart Assoc.* 2015;4:e001424; originally published April 2, 2015;

doi: 10.1161/JAHA.114.001424

The *Journal of the American Heart Association* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Online ISSN: 2047-9980

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://jaha.ahajournals.org/content/4/4/e001424

Data Supplement (unedited) at:

http://jaha.ahajournals.org/content/suppl/2015/04/02/jah3897.DC1.html