

# Heart and Soul and Cardiac Rehabilitation

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**VA**



**U.S. Department of Veterans Affairs**

Veterans Health Administration

*Quality Enhancement Research Initiative*

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## Heart and Soul and Cardiac Rehabilitation



- **Depression associated with adverse cardiovascular outcomes**
- **Key role of health behaviors (especially physical inactivity)**
- **Cardiac rehabilitation an underutilized opportunity to treat both**
- **Ways to improve engagement in cardiac rehabilitation**
- **Potential benefits of COVID pandemic on cardiac rehab delivery**



# Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019



GBD 2019 Diseases and Injuries Collaborators\*

## Summary

**Background** In an era of shifting global agendas and expanded emphasis on non-communicable diseases and injuries along with communicable diseases, sound evidence on trends by cause at the national level is essential. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) provides a systematic scientific assessment of published, publicly available, and contributed data on incidence, prevalence, and mortality for a mutually exclusive and collectively exhaustive list of diseases and injuries.

**Methods** GBD estimates incidence, prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life-years (DALYs) due to 369 diseases and injuries, for two sexes, and for 204 countries and territories. Input data were extracted from censuses, household surveys, civil registration and vital statistics, disease registries, health service use, air pollution monitors, satellite imaging, disease notifications, and other sources. Cause-specific death rates and cause fractions were calculated using the Cause of Death Ensemble model and spatiotemporal Gaussian process regression. Cause-specific deaths were adjusted to match the total all-cause deaths calculated as part of the GBD population, fertility, and mortality estimates. Deaths were multiplied by standard life expectancy at each age to calculate YLLs. A Bayesian meta-regression modelling tool, DisMod-MR 2.1, was used to ensure consistency between incidence, prevalence, remission, excess mortality, and cause-specific mortality for most causes. Prevalence estimates were multiplied by disability weights for mutually exclusive sequelae of diseases and injuries to calculate YLDs. We considered results in the context of the Socio-demographic Index (SDI), a composite indicator of income per capita, years of schooling, and fertility rate in females younger than 25 years. Uncertainty intervals (UIs) were generated for every metric using the 25th and 975th ordered 1000 draw values of the posterior distribution.

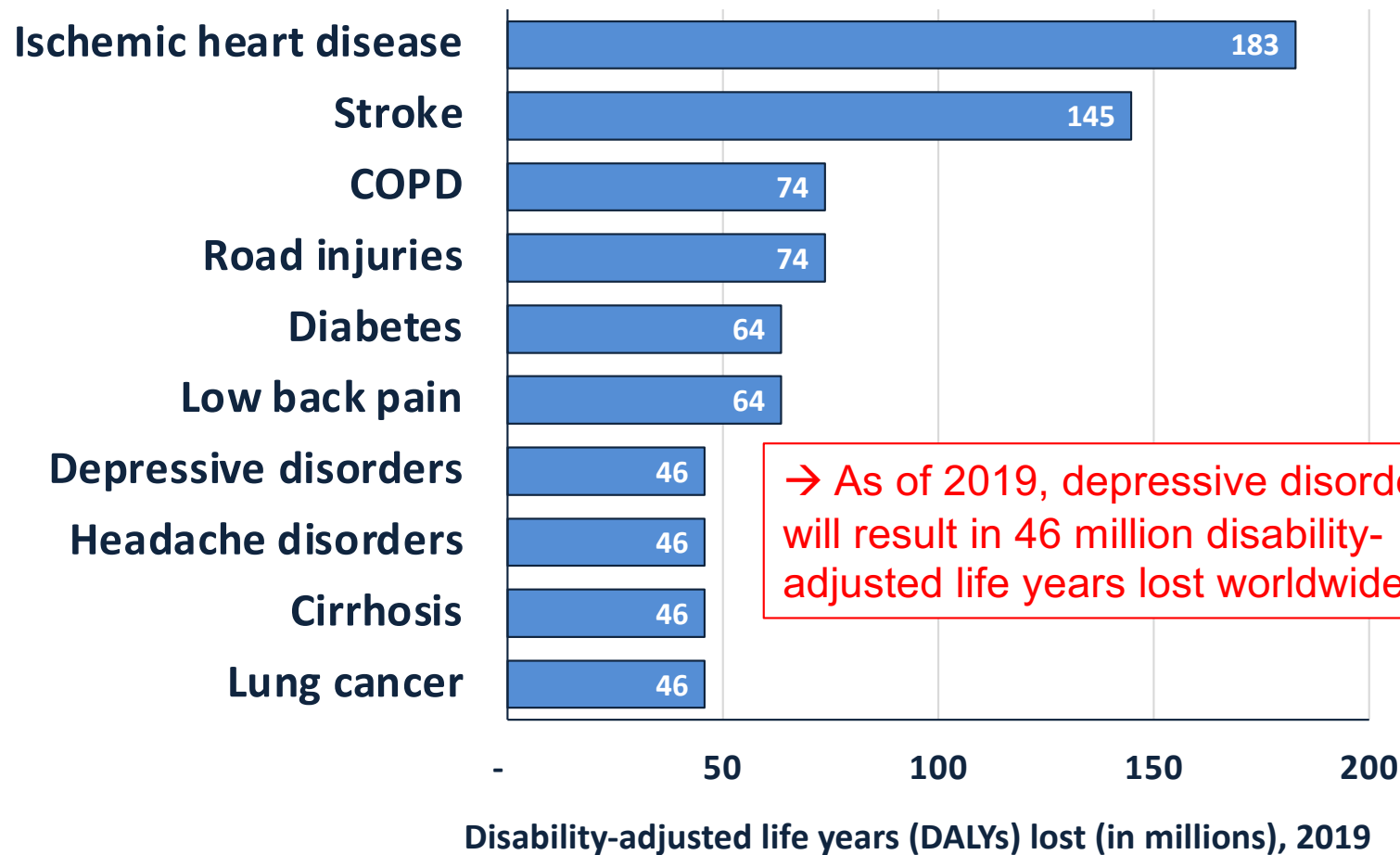
*Lancet* 2020; 396: 1204–22

This online publication has been corrected. The corrected version first appeared at [thelancet.com](https://www.thelancet.com) on October 23, 2020

\*For the list of Collaborators see [Viewpoint Lancet 2020; 396: 1135–59](#)

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# 10 leading (non-communicable) causes of death & disability in adults



*Global Burden of Disease Study, Lancet October 2020; 396: 1204–22.*



EUROPEAN  
SOCIETY OF  
CARDIOLOGY®

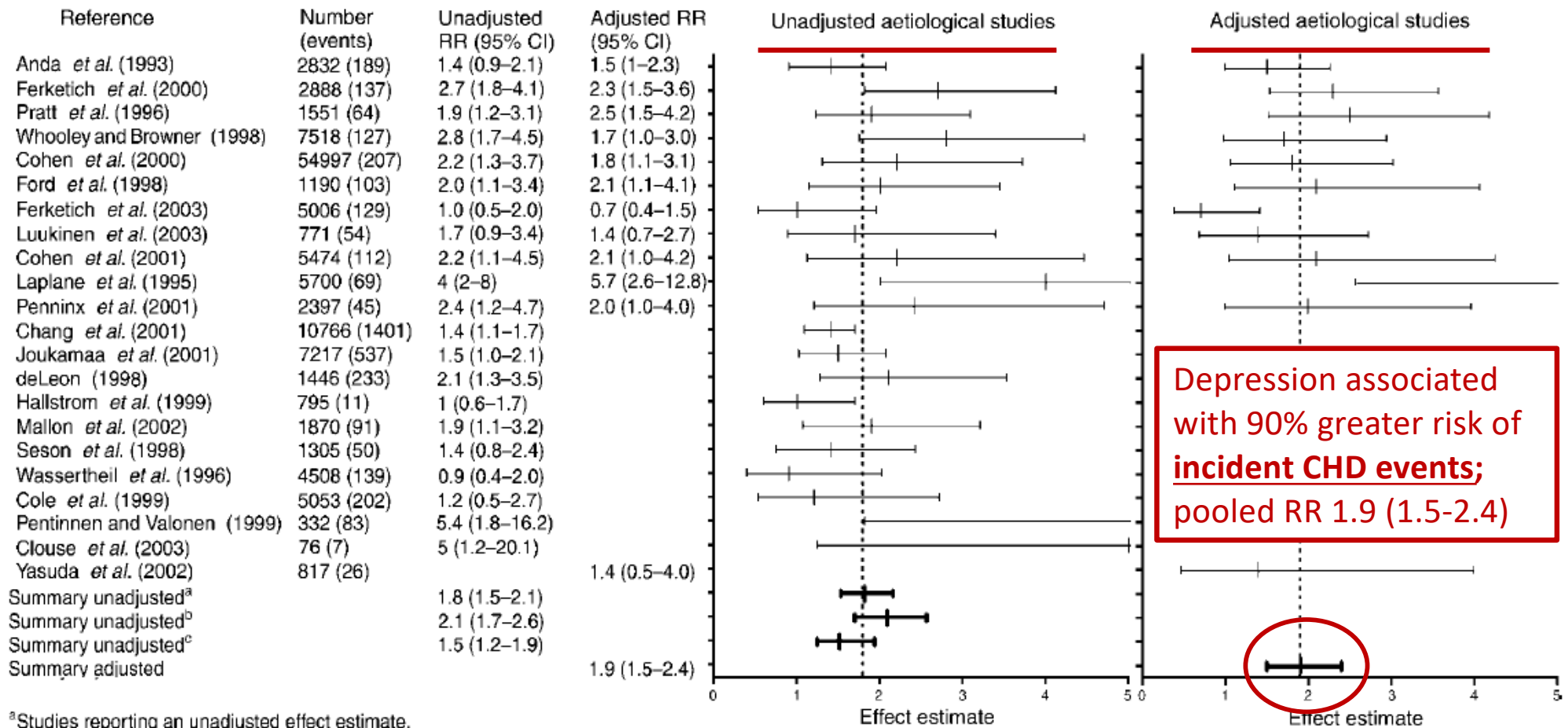
European Heart Journal (2006) 27, 2763–2774  
doi:10.1093/eurheartj/ehl338

Clinical research  
Coronary heart disease

# Depression as an aetiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies

Amanda Nicholson<sup>1\*</sup>, Hannah Kuper<sup>2</sup>, and Harry Hemingway<sup>1</sup>

## Aetiological studies: Forrest plot of the effect of depression on the incidence of CHD



Depression associated with 90% greater risk of incident CHD events; pooled RR 1.9 (1.5-2.4)

<sup>a</sup>Studies reporting an unadjusted effect estimate.

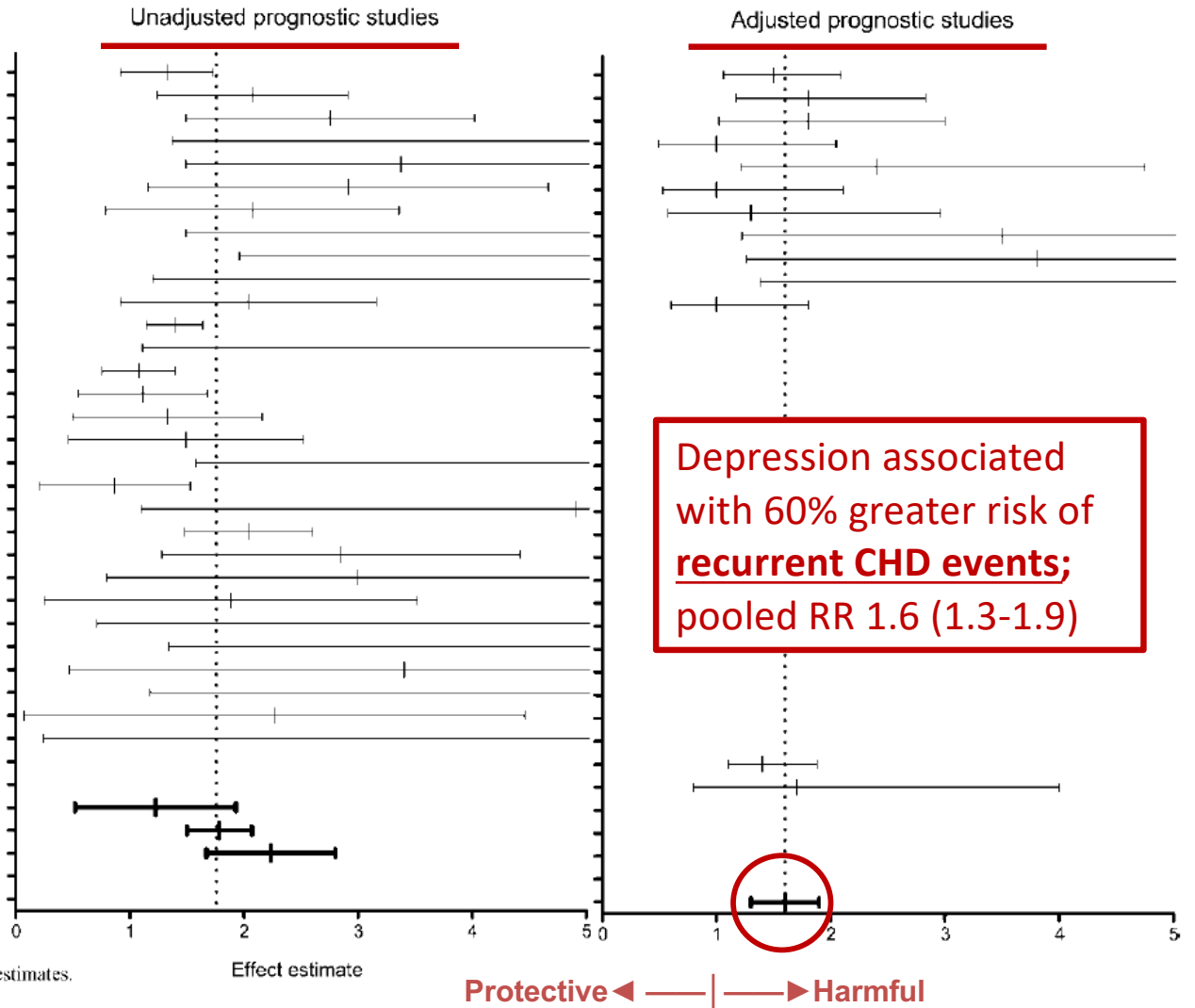
<sup>b</sup>Studies reporting an unadjusted effect estimate that also reported an adjusted effect estimate.

<sup>c</sup>Studies reporting an unadjusted effect estimate that do not reported an adjusted effect estimate.

Protective ← ——— | ——— → Harmful

## Prognostic studies: Forrest plot of the effect of depression on prognosis after CHD

Reference	Number (events)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Blumenthal <i>et al.</i> (2003)	817 (122)	1.3 (0.9–1.7)	1.5 (1.1–2.1)
Penninx <i>et al.</i> (2001)	450 (93)	1.9 (1.2–2.9)	1.8 (1.2–2.8)
Wolin <i>et al.</i> (2000)	267 (67)	2.5 (1.5–4.0)	1.8 (1.0–3.0)
Denollet <i>et al.</i> (1996)	303 (38)	2.4 (1.3–4.4)	1.0 (0.5–2.1)
Carney <i>et al.</i> (2003)	766 (47)	2.8 (1.5–5.3)	2.4 (1.2–4.8)
Kaufmann <i>et al.</i> (1999)	318 (33)	2.3 (1.2–4.7)	1.0 (0.5–2.1)
Lauzon <i>et al.</i> (2003)	550 (28)	1.6 (0.8–3.4)	1.3 (0.6–3.0)
Bush <i>et al.</i> (2001)	267 (17)	3.8 (1.5–9.6)	3.5 (1.2–10.0)
Ladwig <i>et al.</i> (1991)	553 (12)	5.9 (2.0–17.9)	3.8 (1.2–11.6)
Burg <i>et al.</i> (2003)	89 (5)	10.2 (1.2–87.3)	23.2 (1.4–390)
Carinci <i>et al.</i> (1997) <sup>a</sup>	2449 (63)	1.7 (0.9–3.2)	1.0 (0.6–1.8)
Barefoot <i>et al.</i> (1996)	929 (488)	1.4 (1.2–1.6)	
Lesperance <i>et al.</i> (2002)	896 (155)	2.0 (1.5–2.6)	
Moir <i>et al.</i> (1973)	201 (91)	1.0 (0.8–1.4)	
Jenkinson <i>et al.</i> (1993)	1177 (189)	1.0 (0.6–1.7)	
Lane <i>et al.</i> (2002)	288 (38)	1.0 (0.5–2.2)	
Berkman <i>et al.</i> (1992)	187 (73)	1.1 (0.5–2.5)	
Romanelli <i>et al.</i> (2002)	153 (17)	3.8 (1.6–9.1)	
Schleifer <i>et al.</i> (1989)	283 (16)	0.6 (0.2–1.5)	
Thomas <i>et al.</i> (1997)	347 (24)	3.1 (1.1–8.7)	
Lesperance <i>et al.</i> (2000)	430 (16)	3.3 (1.1–9.5)	
Denollet <i>et al.</i> (1995)	105 (15)	4.6 (1.4–15.3)	
Borowicz <i>et al.</i> (2002)	117 (15)	2.0 (0.8–5.2)	
Sullivan <i>et al.</i> (2003)	198 (10)	0.9 (0.3–3.5)	
Peterson <i>et al.</i> (2002)	123 (8)	2.8 (0.7–10.7)	
Denollet and Britsaert (1998)	79 (13)	5.6 (1.3–23.8)	
Shiotani <i>et al.</i> (2002)	1042 (9)	1.7 (0.5–6.3)	
Baker <i>et al.</i> (2001)	158 (6)	6.2 (1.2–33.0)	
Connemey <i>et al.</i> (2001)	309 (8)	0.6 (0.1–4.5)	
Carney <i>et al.</i> (1988)	52 (3)	2.4 (0.2–23.7)	
Bosworth <i>et al.</i> (1999)	2885 (NA)		1.4 (1.1–1.9)
Irvine <i>et al.</i> (1999)	318 (NA)		1.7 (0.8–4.0)
Null		1.0 (0.5–1.9)	
Summary unadjusted <sup>a</sup>		1.8 (1.5–2.1)	
Summary unadjusted <sup>b</sup>		2.2 (1.7–2.8)	
Summary unadjusted <sup>c</sup>		1.5 (1.2–2.0)	
Summary adjusted			1.6 (1.3–1.9)



<sup>a</sup>Studies reporting unadjusted effect estimates.

<sup>b</sup>Studies reporting unadjusted effect estimates that also report an adjusted effect estimates.

# The Heart and Soul Study



- Prospective cohort study of 1017 outpatients with stable coronary disease, enrolled 9/00 – 12/02
- Goal was to determine why depression is associated with adverse cardiovascular outcomes
- Baseline exam included psychiatric interview, blood draw, exercise treadmill, stress echocardiography, 24-hour holter (heart rate variability), and 24-hour urine (catecholamines, cortisol)
- Depressive symptoms assessed using 9-item Patient Health Questionnaire (PHQ)



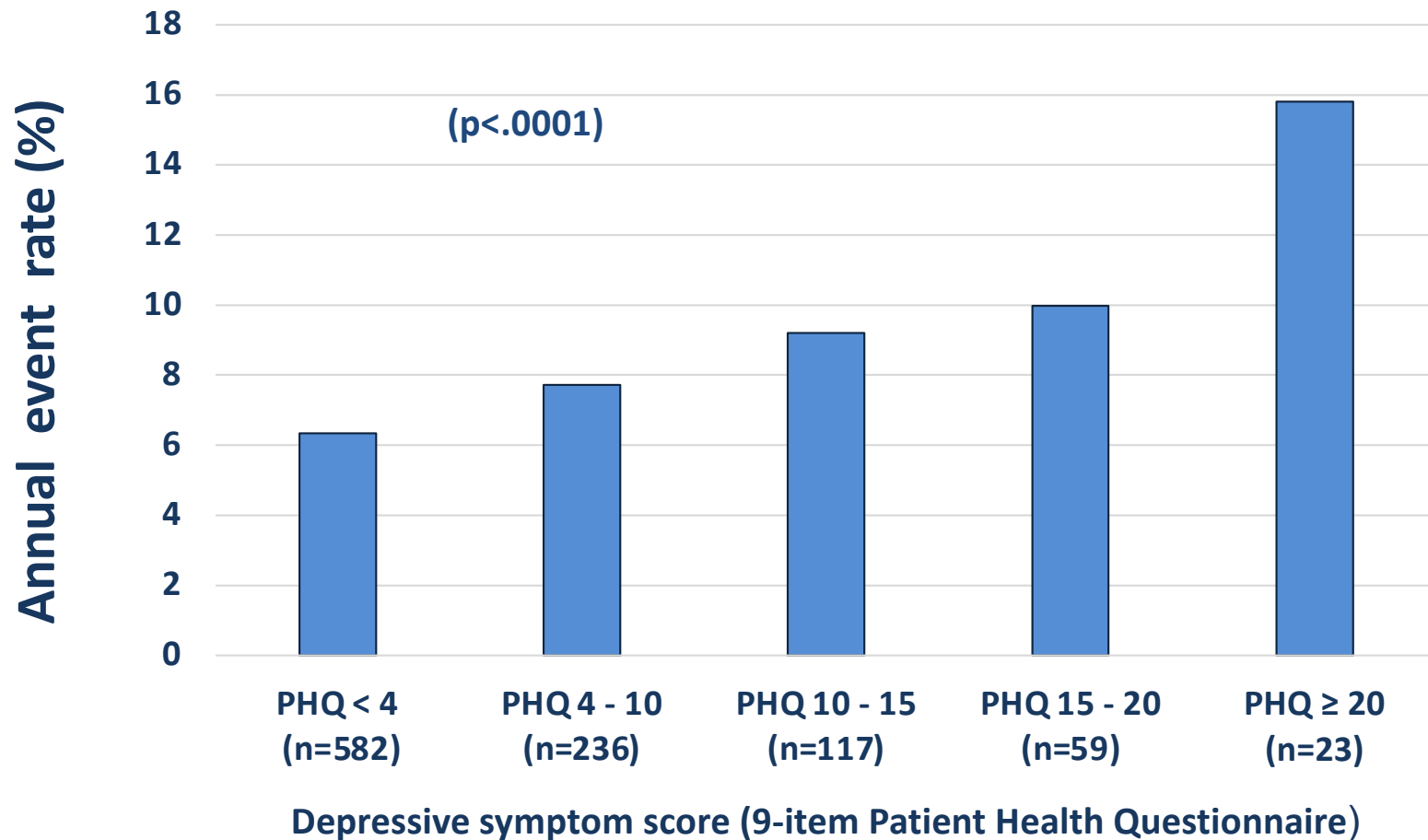
# Heart and Soul Study (1017 patients with coronary heart disease)

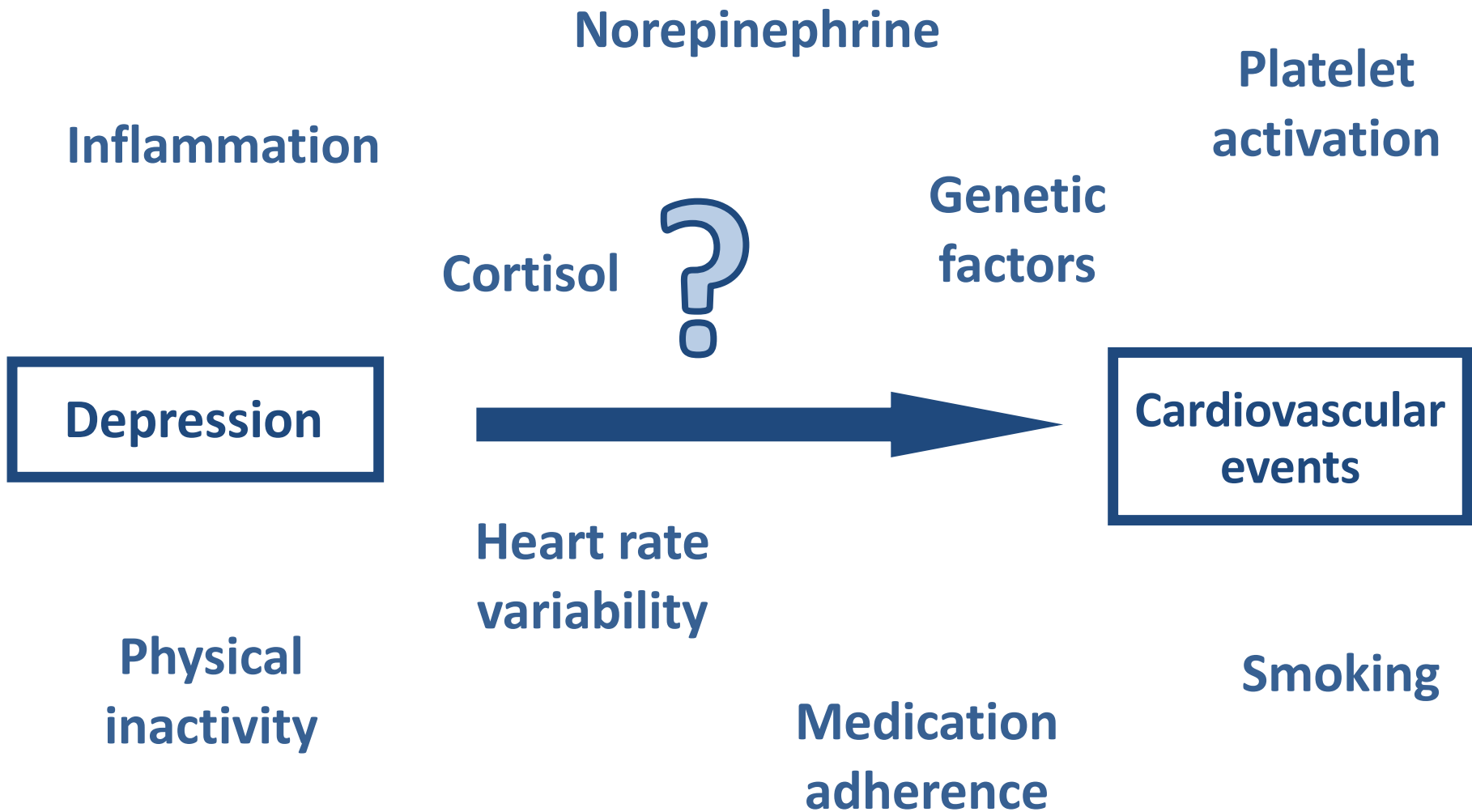


*JAMA*. 2008;300:2379-2388. <https://doi.org/10.1001/jama.2008.711>



## Annual rate of recurrent cardiovascular events (MI, CHF, stroke, or death) during 5-year follow up in 1017 patients





**Depression and Inflammation in Patients With Coronary Heart Disease: Findings from the Heart and Soul Study**  
Mary A. Whooley, Catherine M. Caska, Bethany E. Hendrickson, Meghan A. Rourke, Joseph Ho, and Sadia Ali

**Background:** Depression and inflammation independently predict adverse cardiovascular outcomes in patients with coronary heart disease (CHD). Depression has been associated with elevated levels of inflammation in otherwise healthy patients without known CHD. However, studies investigating the link between depression and inflammation in patients with established CHD have produced inconclusive results.

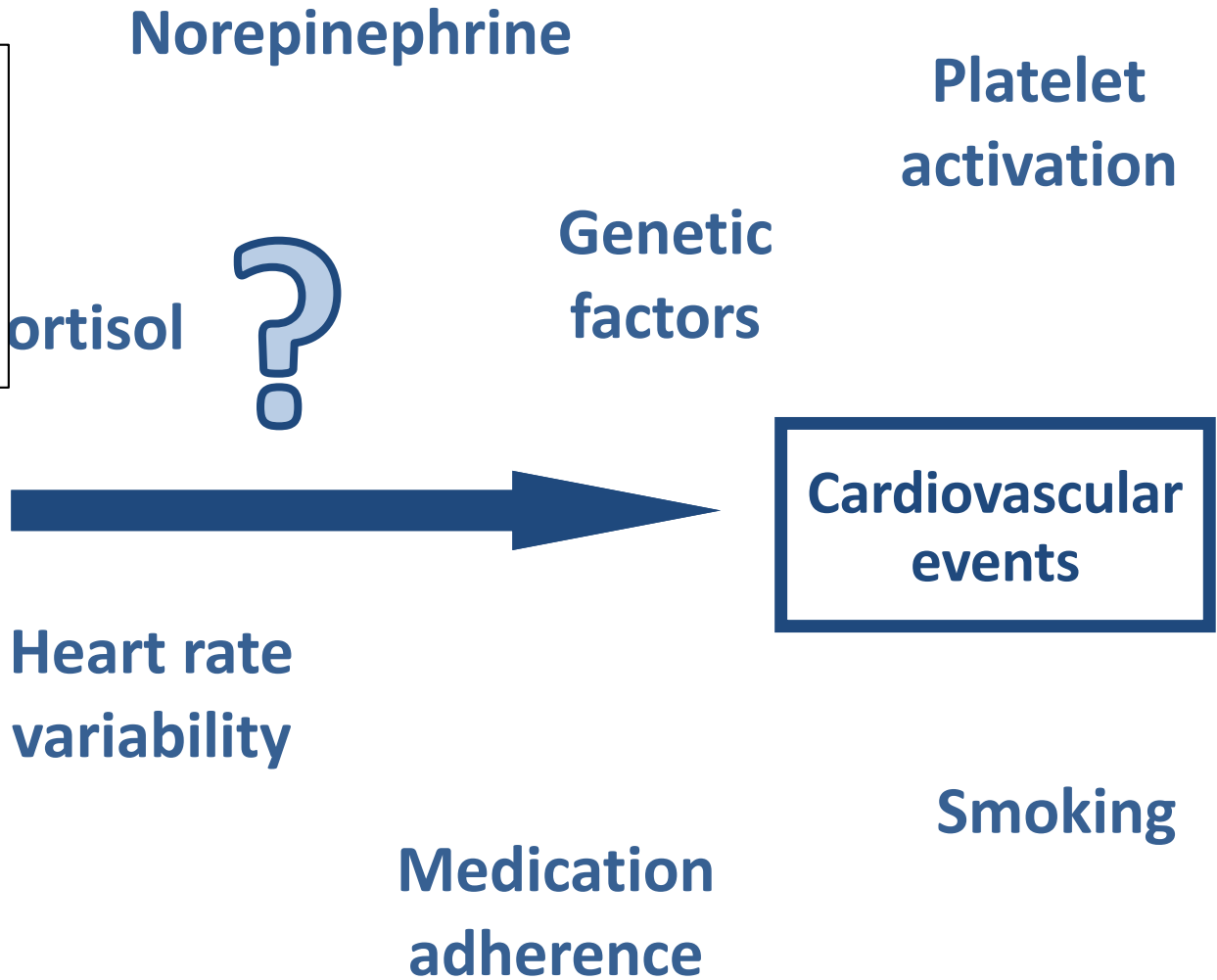
**Methods:** We sought to examine the association of major depression with inflammation in 984 outpatients with established CHD from the Heart and Soul Study. We assessed current major depression with the Computerized Diagnostic Interview Schedule and collected venous blood samples for measurement of five inflammatory biomarkers (white blood cell count, CD40 ligand, C-reactive protein [CRP], fibrinogen, and interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of current depression with inflammatory markers, adjusted for potential confounding variables.

**Results:** Of the 984 participants, 217 (22%) had current major depression. Depression was not associated with increased levels of any inflammatory marker. Contrary to our hypothesis, depression was associated with lower levels of CRP ( $p = .09$ ), fibrinogen ( $p = .006$ ), and IL-6 ( $p = .007$ ) in both unadjusted and adjusted models.

**Conclusions:** We found no evidence that current depression is associated with greater inflammation in outpatients with CHD. Inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with established CHD.

**Depression**

**Physical inactivity**



## Depression and Inflammation in Patient Coronary Heart Disease: Findings from and Soul Study

Mary A. Whooley, Catherine M. Caska, Bethany E. Hendrickson, Meghan A. and Sadia Ali

**Background:** Depression and inflammation independently predict adverse cardiovascular outcomes (CHD). Depression has been associated with elevated levels of inflammation in otherwise healthy patients, but the link between depression and inflammation in patients with established CHD have not been investigated.

**Methods:** We sought to examine the association of major depression with inflammation in 984 outpatients with coronary heart disease (CHD). We assessed current major depression with the Computerized Diagnostic Interview Schedule for Patients (DISC-5.1) and measured five inflammatory biomarkers (white blood cell count, C-reactive protein, interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of depression with inflammation, adjusted for potential confounding variables.

**Results:** Of the 984 participants, 217 (22%) had current major depression. Depression was not associated with inflammation in patients with established CHD. Contrary to our hypothesis, depression was associated with lower levels of CRP ( $p = .007$ ) in both unadjusted and adjusted models.

**Conclusions:** We found no evidence that current depression is associated with greater inflammation in outpatients with CHD. Inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with established CHD.

Article

### Depressive Symptoms and 24-Hour Urinary Norepinephrine Excretion Levels in Patients With Coronary Disease: Findings From the Heart and Soul Study

Christian Otte, M.D.  
Thomas C. Neylan, M.D.  
Sharon S. Pipkin, M.P.H.  
Warren S. Browner, M.D., M.P.H.  
Mary A. Whooley, M.D.

**Objective:** Depressive symptoms are associated with an increased risk of cardiac events in patients with heart disease. Elevated catecholamine levels may contribute to this association, but whether depressive symptoms are associated with catecholamine levels in patients with heart disease is unknown.

**Method:** The authors examined the association between depressive symptoms (defined by a Patient Health Questionnaire score  $\geq 10$ ) and 24-hour urinary norepinephrine, epinephrine, and dopamine excretion levels in 598 subjects with coronary disease.

(65  $\mu\text{g/day}$  versus 59  $\mu\text{g/day}$ , with adjustment for age, sex, body mass index, smoking, urinary creatinine levels, comorbid illnesses, medication use, and cardiac function). In logistic regression analyses, participants with depressive symptoms were more likely than those without depressive symptoms to have norepinephrine excretion levels in the highest quartile and above the normal range. Depressive symptoms were not associated with dopamine or epinephrine excretion levels.

**Conclusions:** In patients with coronary disease, depressive symptoms are associated with elevated levels of urinary norepinephrine excretion.

## Depression and 24-Hour Urinary Cortisol in Medical Outpatients with Coronary Heart Disease: The Heart and Soul Study

Christian Otte, Charles R. Marmar, Sharon S. Pipkin, Rudolf Moos, Warren S. Browner, and Mary A. Whooley

**Background:** In patients with coronary heart disease (CHD), depression leads to worse cardiovascular outcomes. Depression has been associated with increased cortisol in medically healthy patients, suggesting that cortisol may act as a mediator in the pathway between depression and cardiovascular events. However, it is not known whether depression is associated with elevated cortisol levels in patients with CHD.

**Methods:** We examined the association between depression (assessed by the Computerized Diagnostic Interview Schedule) and 24-hour urinary cortisol in 693 medical outpatients with known CHD.

**Results:** Of 693 participants, 138 (20%) had current depression. Depressed participants had greater mean cortisol levels than those without depression ( $42 \pm 25$  vs.  $35 \pm 20$   $\mu\text{g/day}$ ,  $p < .01$ ). With each increasing quartile of cortisol concentration the frequency of depression increased ( $p < .01$ ). Participants in the highest quartile of cortisol had a twofold increased odds of having depression, compared with those in the lowest quartile (odds ratio [OR] 2.1, 95% confidence interval [CI] 1.2-3.6,  $p = .01$ ). This association remained strong after adjusting for potential confounding variables (OR 2.4, 95% CI 1.3-4.4,  $p < .01$ ). In this cross-sectional analysis, elevated cortisol was not associated with worse cardiac function.

**Conclusions:** In patients with CHD, depression is associated with elevated cortisol levels.

norepinephrine

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### Psychiatry Research

journal homepage: [www.elsevier.com/locate/psychres](http://www.elsevier.com/locate/psychres)

## Depression and platelet activation in outpatients with stable coronary heart disease: Findings from the Heart and Soul Study

Anil Gehi <sup>a</sup>, Dominique Musselman <sup>b</sup>, Christian Otte <sup>c</sup>, Erica Bruce Royster <sup>b</sup>, Sadia Ali <sup>d</sup>, Mary A. Whooley <sup>d,e,f,\*</sup>

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factors

Depression

Cardiovascular events

Heart rate variability

Physical inactivity

Smoking

Medication adherence

## Depression and Inflammation in Patients With Coronary Heart Disease: Findings from the Heart and Soul Study

Mary A. Whooley, Catherine M. Caska, Bethany E. Hendrickson, Meghan A. and Sadia Ali

**Background:** Depression and inflammation independently predict adverse cardiovascular outcomes (CHD). Depression has been associated with elevated levels of inflammation in otherwise healthy patients. Investigating the link between depression and inflammation in patients with established CHD have previously.

**Methods:** We sought to examine the association of major depression with inflammation in 984 outpatients with CHD. We assessed current major depression with the Computerized Diagnostic Interview Schedule (DISC) and blood samples for measurement of five inflammatory biomarkers (white blood cell count, CD40 ligand, and interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of markers, adjusted for potential confounding variables.

**Results:** Of the 984 participants, 217 (22%) had current major depression. Depression was not associated with inflammation. Contrary to our hypothesis, depression was associated with lower levels of CRP ( $p = .007$ ) in both unadjusted and adjusted models.

**Conclusions:** We found no evidence that current depression is associated with greater inflammation in outpatients with CHD. Inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with established CHD.

## Article

### Depressive Symptoms and 24-Hour Urinary Norepinephrine Excretion Levels in Patients With Coronary Disease: Findings From the Heart and Soul Study

Christian Otte, M.D.  
Thomas C. Neylan, M.D.  
Sharon S. Pipkin, M.P.H.  
Warren S. Browner, M.D., M.P.H.  
Mary A. Whooley, M.D.

**Objective:** Depressive symptoms are associated with an increased risk of cardiac events in patients with heart disease. Elevated catecholamine levels may contribute to this association, but whether depressive symptoms are associated with catecholamine levels in patients with heart disease is unknown.

**Method:** The authors examined the association between depressive symptoms (defined by a Patient Health Questionnaire score  $\geq 10$ ) and 24-hour urinary norepinephrine, epinephrine, and dopamine excretion levels in 598 subjects with coronary disease.

(65  $\mu\text{g/day}$  versus 59  $\mu\text{g/day}$ , with adjustment for age, sex, body mass index, smoking, urinary creatinine levels, comorbidities, medication use, and cardiac function). In logistic regression analysis, participants with depressive symptoms were more likely than those without depressive symptoms to have norepinephrine excretion levels in the highest quartile and above the normal range. Depressive symptoms were not associated with epinephrine or dopamine excretion levels.

**Conclusions:** In patients with coronary disease, depressive symptoms are associated with elevated norepinephrine excretion levels.

### Depression and 24-Hour Urinary Cortisol in Medically Healthy Outpatients with Coronary Heart Disease and the Heart and Soul Study

Christian Otte, Charles R. Marmar, Sharon S. Pipkin, Rudolf Moos, Warren S. Browner, M.D., M.P.H., and Mary A. Whooley

**Background:** In patients with coronary heart disease (CHD), depression leads to worse cardiovascular outcomes. Elevated cortisol levels are associated with increased risk of cardiovascular events. However, it is not known whether depression is associated with elevated cortisol levels in medically healthy patients.

**Methods:** We examined the association between depression (assessed by the Computerized Diagnostic Interview Schedule) and 24-hour urinary cortisol in 651 medically healthy outpatients with known CHD.

**Results:** Of 651 participants, 158 (24%) had current depression. Depressed participants had higher 24-hour urinary cortisol levels ( $42 \pm 25$  vs.  $35 \pm 20$   $\mu\text{g/day}$ ,  $p < .01$ ). With each increasing quartile of cortisol concentration the frequency of depression increased ( $p < .01$ ). Participants in the highest quartile of cortisol had a twofold increased odds of having depression, compared with those in the lowest quartile (odds ratio [OR] 2.1, 95% confidence interval [CI] 1.2-3.6,  $p = .01$ ). This association remained strong after adjusting for potential confounding variables (OR 2.4, 95% CI 1.3-4.4,  $p < .01$ ). In this cross-sectional analysis, elevated cortisol was not associated with worse cardiac function.

**Conclusions:** In patients with CHD, depression is associated with elevated cortisol levels.

## Article

### Association of a Serotonin Transporter Polymorphism (5-HTTLPR) With Depression, Perceived Stress, and Norepinephrine in Patients With Coronary Disease: The Heart and Soul Study

Christian Otte, M.D.  
Jeanne McCaffery, Ph.D.  
Sadia Ali, M.P.H.  
Mary A. Whooley, M.D.

**Objective:** The short allele of a functional polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) has been shown to interact with stressful life events to predict depression in otherwise healthy individuals. Whether the short allele increases risk for depression associated with the stress of a chronic illness has not been established.

**Method:** In a cross-sectional genetic association study, the authors examined the association of 5-HTTLPR with current depression (measured by the Computerized Diagnostic Interview Schedule), perceived stress (measured by the Perceived Stress Scale), and 24-hour urinary norepinephrine excretion in 557 outpatients with chronic coronary disease.

**Results:** Among individuals carrying an s allele, 25% (97 of 383) had current depression, compared with 17% (29 of 174) of ll homozygotes. The unadjusted odds

ratio was 1.6, with a 95% confidence interval (CI) of 1.0-2.6; the age- and gender-adjusted odds ratio was also 1.6 (95% CI=1.0-2.5). Participants carrying an s allele had a higher mean score for perceived stress than ll homozygotes (5.4 versus 4.7) and a higher rate of moderate or high perceived stress (adjusted odds ratio=1.6, 95% CI=1.1-2.3). Mean 24-hour norepinephrine excretion was higher in s allele carriers (55.6 versus 50.2  $\mu\text{g/day}$ ), who were more likely to have norepinephrine values in the highest quartile (adjusted odds ratio=1.7, 95% CI=1.0-3.0).

**Conclusions:** Among patients with chronic illness, carriers of the s allele of 5-HTTLPR are more vulnerable to depression, perceived stress, and high norepinephrine secretion. These factors may contribute to worse cardiovascular outcomes in these patients.

[Am J Psychiatry 2009;166:1000-1006]

outpatients with stable coronary heart disease: a cross-sectional study

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Depression

Cardiovascular events

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## Depression and Inflammation in Patient Coronary Heart Disease: Findings from and Soul Study

Mary A. Whooley, Catherine M. Caska, Bethany E. Hendrickson, Meghan A. and Sadia Ali

**Background:** Depression and inflammation independently predict adverse cardiovascular outcomes (CHD). Depression has been associated with elevated levels of inflammation in otherwise healthy patients. We investigated the link between depression and inflammation in patients with established CHD have pr

**Methods:** We sought to examine the association of major depression with inflammation in 984 outpatients with Heart and Soul Study. We assessed current major depression with the Computerized Diagnostic Interview Schedule (DISC) and blood samples for measurement of five inflammatory biomarkers (white blood cell count, CD40 ligand, and interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of markers, adjusted for potential confounding variables.

**Results:** Of the 984 participants, 217 (22%) had current major depression. Depression was not associated with inflammation. Contrary to our hypothesis, depression was associated with lower levels of CRP ( $p = .007$ ) in both unadjusted and adjusted models.

**Conclusions:** We found no evidence that current depression is associated with greater inflammation in outpatients with CHD. Inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with established CHD.

Christian Otte, M.D.  
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**Objective:** Depressive symptoms are associated with an increased risk of cardiac events in patients with heart disease. Elevated catecholamine levels may contribute to this association, but whether depressive symptoms are associated with catecholamine levels in patients with heart disease is unknown.

**Method:** The authors examined the association between depressive symptoms (defined by a Patient Health Questionnaire score  $\geq 10$ ) and 24-hour urinary norepinephrine, epinephrine, and dopamine excretion levels in 598 subjects with coronary disease.

**Results:** Depressive symptoms were associated with higher levels of norepinephrine excretion (mean  $59 \mu\text{g/day}$  versus  $65 \mu\text{g/day}$  versus  $59 \mu\text{g/day}$ , with adjustment for age, sex, body mass index, smoking, urinary creatinine levels, comorbidities, medication use, and cardiac function). In logistic regression analysis, participants with depressive symptoms were more likely than those without depressive symptoms to have norepinephrine excretion levels in the highest quartile and above the normal range. Depressive symptoms were not associated with dopamine or epinephrine excretion levels.

**Conclusions:** In patients with coronary disease, depressive symptoms are associated with higher levels of norepinephrine excretion.

## Depression and 24-Hour Urinary Cortisol Outpatients with Coronary Heart Disease and Soul Study

Christian Otte, Charles R. Marmar, Sharon S. Pipkin, Rudolf Moos, Warren S. Browner, M.D., M.P.H., Mary A. Whooley

**Background:** In patients with coronary heart disease (CHD), depression leads to worse cardiovascular outcomes. It is not known whether depression is associated with increased cortisol in medically healthy patients, suggesting that cortisol mediates the association between depression and cardiovascular events. However, it is not known whether depression is associated with CHD.

**Methods:** We examined the association between depression (assessed by the Computerized Diagnostic Interview Schedule) and 24-hour urinary cortisol in 695 medical outpatients with known CHD.

**Results:** Of 695 participants, 138 (20%) had current depression. Depressed participants had higher levels of cortisol (mean  $42 \pm 25$  vs.  $35 \pm 20 \mu\text{g/day}$ ,  $p < .01$ ). With each increasing quartile of cortisol concentration the frequency of depression increased ( $p < .01$ ). Participants in the highest quartile of cortisol had a twofold increased odds of having depression, compared with those in the lowest quartile (odds ratio 2.1, 95% confidence interval [CI] 1.2-3.6,  $p = .01$ ). This association

ORIGINAL ARTICLE

## Depression and Heart Rate Variability in Patients With Stable Coronary Heart Disease

Findings From the Heart and Soul Study

Anil Gehi, MD; Dennis Mangano, PhD, MD; Sharon Pipkin, MPH; Warren S. Browner, MD, MPH; Mary A. Whooley, MD

**Context:** Depression is associated with low heart rate variability (HRV) in patients following myocardial infarction, suggesting that alterations in the autonomic nervous system may contribute to the adverse cardiac outcomes associated with depression. Whether depression is associated with low HRV in patients with stable coronary heart disease (CHD) is not known.

**Objective:** To examine the association between major depression and 24-hour HRV in patients with stable CHD.

**Design, Setting, and Participants:** Cross-sectional study of 873 outpatients with stable CHD recruited from outpatient clinics in the San Francisco Bay Area, California.

**Main Outcome Measures:** Major depression was assessed using the Computerized National Institute of Mental Health Diagnostic Interview Schedule. Heart rate variability was measured by 24-hour ambulatory electrocardiography.

rate variability was measured by 24-hour ambulatory electrocardiography.

**Results:** A total of 195 participants (22%) had major depression. Overall, we observed no association between depression and HRV as measured by time domain or frequency domain variables. Mean HRV was similar in participants with and without depression (all  $P$  values  $> .10$ ), and participants with depression were no more likely than those without depression to have low HRV (all  $P$  values  $> .10$ ).

**Conclusions:** We found no evidence of an association between depression and HRV in 873 outpatients with stable CHD. These findings raise questions about the potential role of HRV in the association between depression and cardiovascular disease.

Arch Gen Psychiatry. 2005;62:661-666

## Depressive Symptoms and 24-Hour Urinary Norepinephrine Excretion Levels in Patients With Coronary Disease: Findings From the Heart and Soul Study

Christian Otte, M.D.  
Thomas C. Neylan, M.D.  
Sharon S. Pipkin, M.P.H.  
Warren S. Browner, M.D., M.P.H.  
Mary A. Whooley, M.D.

**Objective:** Depressive symptoms are associated with an increased risk of cardiac events in patients with heart disease. Elevated catecholamine levels may contribute to this association, but whether depressive symptoms are associated with catecholamine levels in patients with heart disease is unknown.

**Method:** The authors examined the association between depressive symptoms (defined by a Patient Health Questionnaire score  $\geq 10$ ) and 24-hour urinary norepinephrine, epinephrine, and dopamine excretion levels in 598 subjects with coronary disease.

**Results:** Depressive symptoms were associated with higher levels of norepinephrine excretion (mean  $59 \mu\text{g/day}$  versus  $65 \mu\text{g/day}$  versus  $59 \mu\text{g/day}$ , with adjustment for age, sex, body mass index, smoking, urinary creatinine levels, comorbidities, medication use, and cardiac function). In logistic regression analysis, participants with depressive symptoms were more likely than those without depressive symptoms to have norepinephrine excretion levels in the highest quartile and above the normal range. Depressive symptoms were not associated with dopamine or epinephrine excretion levels.

**Conclusions:** In patients with coronary disease, depressive symptoms are associated with higher levels of norepinephrine excretion.

## Association of a Serotonin Transporter Polymorphism (5-HTTLPR) With Depression, Perceived Stress, and Norepinephrine in Patients With Coronary Disease: The Heart and Soul Study

Christian Otte, M.D.  
Jeanne McCaffery, Ph.D.  
Sadia Ali, M.P.H.  
Mary A. Whooley, M.D.

**Objective:** The short allele of a functional polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) has been shown to interact with stressful life events to predict depression in otherwise healthy individuals. Whether the short allele increases risk for depression associated with the stress of a chronic illness has not been established.

**Method:** In a cross-sectional genetic association study, the authors examined the association of 5-HTTLPR with current depression (measured by the Computerized Diagnostic Interview Schedule), perceived stress (measured by the Perceived Stress Scale), and 24-hour urinary norepinephrine excretion in 557 outpatients with chronic coronary disease.

**Results:** Among individuals carrying an s allele, 25% (97 of 383) had current depression, compared with 17% (29 of 174) of ll homozygotes. The unadjusted odds

ratio was 1.6, with a 95% confidence interval (CI) of 1.0-2.6; the age- and gender-adjusted odds ratio was also 1.6 (95% CI = 1.0-2.5). Participants carrying an s allele had a higher mean score for perceived stress than ll homozygotes (5.4 versus 4.7) and a higher rate of moderate or high perceived stress (adjusted odds ratio = 1.6, 95% CI = 1.1-2.3). Mean 24-hour norepinephrine excretion was higher in s allele carriers (55.6 versus 50.2  $\mu\text{g/day}$ ), who were more likely to have norepinephrine values in the highest quartile (adjusted odds ratio = 1.7, 95% CI = 1.0-3.0).

**Conclusions:** Among patients with chronic illness, carriers of the s allele of 5-HTTLPR are more vulnerable to depression, perceived stress, and high norepinephrine secretion. These factors may contribute to worse cardiovascular outcomes in these patients.

Am J Psychiatry

Depression

Cardiovascular events

## Relation Between Depressive Symptoms and Treadmill Exercise Capacity in the Heart and Soul Study

Bernice Ruo, MD, John S. Rumsfeld, MD, PhD, Sharon Pipkin, MPH, and Mary A. Whooley, MD

To examine the association between depressive symptoms and exercise capacity, we performed a cross-sectional study of 944 outpatients with stable coronary artery disease and found that the presence of depressive symptoms was independently associated with poor exercise capacity ( $< 5$  MET tasks achieved; adjusted odds ratio 1.8, 95% confidence interval 1.1 to 2.7,  $p = 0.01$ ). Depressive symptoms should be considered in the differential diagnosis of poor exercise capacity. ©2004 by Excerpta Medica, Inc.

(Am J Cardiol 2004;94:96-99)

Our goal in this study was to examine the relation between depressive symptoms and treadmill exercise capacity in 944 patients with stable coronary artery disease (CAD). We hypothesized that depressive symptoms would be associated with lower exercise capacity. This protocol was approved by the appropriate institutional review board. Each participant provided written, informed consent.

Each participant underwent a symptom-limited treadmill test according to the Bruce protocol. To achieve maximum heart rate, participants who were unable to continue the Bruce protocol (for orthopedic or other reasons) were tested on a treadmill at a slower speed and as long as possible. Maximum exercise capacity was calculated as the total number of METs achieved. Beforehand, we categorized participants into those with poor ( $< 5$  METs) and normal ( $\geq 5$  METs) exercise capacity.<sup>2</sup> To calculate percent maximum heart rate achieved, the maximum heart rate achieved was divided by  $(220 - \text{age})$ .

Smoking  
Medication adherence



## Depression and Inflammation in Patient Coronary Heart Disease: Findings from and Soul Study

Mary A. Whooley, Catherine M. Caska, Bethany E. Hendrickson, Meghan A. and Sadia Ali

**Background:** Depression and inflammation independently predict adverse cardiovascular outcomes (CHD). Depression has been associated with elevated levels of inflammation in otherwise healthy patients. Investigating the link between depression and inflammation in patients with established CHD have pr

**Methods:** We sought to examine the association of major depression with inflammation in 984 outpatients with Heart and Soul Study. We assessed current major depression with the Computerized Diagnostic Interview Schedule for measurement of five inflammatory biomarkers (white blood cell count, CD40 ligand, and interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of markers, adjusted for potential confounding variables.

**Results:** Of the 984 participants, 217 (22%) had current major depression. Depression was not an inflammatory marker. Contrary to our hypothesis, depression was associated with lower levels of CRP ( $p = .007$ ) in both unadjusted and adjusted models.

**Conclusions:** We found no evidence that current depression is associated with greater inflammation in outpatients with CHD. Inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with established CHD.

## Depressive Symptoms and 24-Hour Urinary Norepinephrine Excretion Levels in Patients With Coronary Disease: Findings From the Heart and Soul Study

Christian Otte, M.D.  
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Mary A. Whooley, M.D.

**Objective:** Depressive symptoms are associated with an increased risk of cardiac events in patients with heart disease. Elevated catecholamine levels may contribute to this association, but whether depressive symptoms are associated with catecholamine levels in patients with heart disease is unknown.

**Method:** The authors examined the association between depressive symptoms (defined by a Patient Health Questionnaire score  $\geq 10$ ) and 24-hour urinary norepinephrine, epinephrine, and dopamine excretion levels in 598 subjects with coronary disease.

(65  $\mu\text{g/day}$  versus 59  $\mu\text{g/day}$ , with adjustment for age, sex, body mass index, smoking, urinary creatinine levels, comorbidities, medication use, and cardiac function). In logistic regression analysis, participants with depressive symptoms were more likely than those without depressive symptoms to have norepinephrine excretion levels in the highest quartile and above the normal range. Depressive symptoms were not associated with dopamine or epinephrine excretion levels.

**Conclusions:** In patients with coronary disease, depressive symptoms are associated with higher levels of norepinephrine excretion.

## Depression and 24-Hour Urinary Cortisol Outpatients with Coronary Heart Disease and Soul Study

Christian Otte, Charles R. Marmar, Sharon S. Pipkin, Rudolf Moos, Warren S. Browner, M.D., M.P.H., Mary A. Whooley

**Background:** In patients with coronary heart disease (CHD), depression leads to worse cardiovascular outcomes. Depression is associated with increased cortisol in medically healthy patients, suggesting that cortisol mediates the association between depression and cardiovascular events. However, it is not known whether depression is associated with CHD.

**Methods:** We examined the association between depression (assessed by the Computerized Diagnostic Interview Schedule) and 24-hour urinary cortisol in 695 medical outpatients with known CHD.

**Results:** Of 695 participants, 138 (20%) had current depression. Depressed participants had higher 24-hour urinary cortisol levels ( $42 \pm 25$  vs.  $35 \pm 20$   $\mu\text{g/day}$ ,  $p < .01$ ). With each increasing quartile of cortisol concentration the frequency of depression increased ( $p < .01$ ). Participants in the highest quartile of cortisol had a twofold increased odds of having depression, compared with those in the lowest quartile (odds ratio 2.0, 95% confidence interval 1.3-3.1,  $p = .01$ ). This association

ORIGINAL ARTICLE

## Depression and Heart Rate Variability in Patients With Stable Coronary Heart Disease

Findings From the Heart and Soul Study

Anil Gehi, MD; Dennis Mangano, PhD, MD; Sharon Pipkin, MPH; Warren S. Browner, MD, MPH; Mary A. Whooley, MD

**Context:** Depression is associated with low heart rate variability (HRV) in patients following myocardial infarction, suggesting that alterations in the autonomic nervous system may contribute to the adverse cardiac outcomes associated with depression. Whether depression is associated with low HRV in patients with stable coronary heart disease (CHD) is not known.

**Objective:** To examine the association between major depression and 24-hour HRV in patients with stable CHD.

**Design, Setting, and Participants:** Cross-sectional study of 873 outpatients with stable CHD recruited from outpatient clinics in the San Francisco Bay Area, California.

**Main Outcome Measures:** Major depression was assessed using the Computerized Diagnostic Interview Schedule. Heart rate variability was measured using 24-hour ambulatory electrocardiography.

**Results:** A total of 195 depressed patients were identified. Overall, we observed a significant association between depression and HRV as measured by 24-hour ambulatory electrocardiography. Mean 24-hour HRV was lower in depressed patients with depression than in those without depression to be

**Conclusions:** We found a significant association between depression and low 24-hour HRV in patients with stable CHD. These findings suggest that depression may play a role in the pathogenesis of CHD. Arch Gen Psychiatry. 2005;162:2508-2513.

## Association of a Serotonin Transporter Polymorphism (5-HTTLPR) With Depression, Perceived Stress, and Norepinephrine in Patients With Coronary Disease: The Heart and Soul Study

Christian Otte, M.D.  
Jeanne McCaffery, Ph.D.  
Sadia Ali, M.P.H.  
Mary A. Whooley, M.D.

**Objective:** The short allele of a functional polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) has been shown to interact with stressful life events to predict depression in otherwise healthy individuals. Whether the short allele increases risk for depression associated with the stress of a chronic illness has not been established.

**Method:** In a cross-sectional genetic association study, the authors examined the association of 5-HTTLPR with current depression (measured by the Computerized Diagnostic Interview Schedule), perceived stress (measured by the Perceived Stress Scale), and 24-hour urinary norepinephrine excretion in 557 outpatients with chronic coronary disease.

**Results:** Among individuals carrying an s allele, 25% (97 of 383) had current depression, compared with 17% (29 of 174) of ll homozygotes. The unadjusted odds

ratio was 1.6, with a 95% confidence interval (CI) of 1.0-2.6; the age- and gender-adjusted odds ratio was also 1.6 (95% CI = 1.0-2.5). Participants carrying an s allele had a higher mean score for perceived stress than ll homozygotes (5.4 versus 4.7) and a higher rate of moderate or high perceived stress (adjusted odds ratio = 1.6, 95% CI = 1.1-2.3). Mean 24-hour norepinephrine excretion was higher in s allele carriers (55.6 versus 50.2  $\mu\text{g/day}$ ), who were more likely to have norepinephrine values in the highest quartile (adjusted odds ratio = 1.7, 95% CI = 1.0-3.0).

**Conclusions:** Among patients with chronic illness, carriers of the s allele of 5-HTTLPR are more vulnerable to depression, perceived stress, and high norepinephrine secretion. These factors may contribute to worse cardiovascular outcomes in these patients.

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outpatients with stable coronary heart disease: a study

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# Depression

# Cardiovascular events

## Relation Between Depressive Symptoms and Treadmill Exercise Capacity in the Heart and Soul Study

Bernice Ruo, MD, John S. Rumsfeld, MD, PhD, Sharon Pipkin, MPH, and Mary A. Whooley, MD

To examine the association between depressive symptoms and exercise capacity, we performed a cross-sectional study of 944 outpatients with stable coronary artery disease and found that the presence of depressive symptoms was independently associated with poor exercise capacity (<5 MET tasks achieved; adjusted odds ratio 1.8, 95% confidence interval 1.1 to 2.7,  $p = 0.01$ ). Depressive symptoms should be considered in the differential diagnosis of poor exercise capacity. ©2004 by Excerpta Medica, Inc.

[Am J Cardiol 2004;94:96-99]

Our goal in this study was to examine the relation between depressive symptoms and treadmill exercise capacity in 944 patients with stable coronary artery disease (CAD). We hypothesized that depressive

symptoms would be associated with lower exercise capacity. We performed the exercise treadmill test. Level of exercise capacity was defined as the maximum heart rate achieved divided by (220 - age).

Each participant underwent a symptom-limited exercise treadmill test according to the Bruce protocol. To achieve maximum heart rate, participants who were unable to continue the Bruce protocol (for orthopedic or other reasons) were switched to slower settings on the treadmill and encouraged to exercise for as long as possible. Exercise capacity was calculated as the total number of METs achieved. Beforehand, we categorized participants into those with poor (<5 METs) and normal ( $\geq 5$  METs) exercise capacity. To calculate percent maximum heart rate achieved, the maximum heart rate achieved was divided by (220 - age).

## Depression and Medication Adherence in Outpatients With Coronary Heart Disease

Findings From the Heart and Soul Study

Anil Gehi, MD; Donald Haas, MD, MPH; Sharon Pipkin, MPH; Mary A. Whooley, MD

**Background:** Depression leads to adverse outcomes in patients with coronary heart disease (CHD). Medication nonadherence is a potential mechanism for the increased risk of CHD events associated with depression, but it is not known whether depression is associated with medication nonadherence in outpatients with stable CHD.

**Methods:** We examined the association between current major depression (assessed using the Diagnostic Interview Schedule) and self-reported medication adherence in a cross-sectional study of 940 outpatients with stable CHD.

**Results:** A total of 204 participants (22%) had major depression. Twenty-eight (14%) of 204 depressed participants reported not taking their medications as prescribed compared with 40 (3%) of 736 nondepressed participants (odds ratio [OR], 2.8; 95% confidence interval [CI], 1.7-4.7;  $P < .001$ ). Twice as many depressed

participants as nondepressed participants (18% vs 9%) reported forgetting to take their medications (OR, 2.4; 95% CI, 1.6-3.8;  $P < .001$ ). Nine percent of depressed participants and 4% of nondepressed participants reported deciding to skip their medications (OR, 2.2; 95% CI, 1.2-4.2;  $P = .01$ ). The relationship between depression and nonadherence persisted after adjustment for potential confounding variables, including age, ethnicity, education, social support, and measures of cardiac disease severity (OR, 2.2; 95% CI, 1.2-3.9;  $P = .009$  for not taking medications as prescribed).

**Conclusions:** Depression is associated with medication nonadherence in outpatients with CHD. Medication nonadherence may contribute to adverse cardiovascular outcomes in depressed patients.

Arch Intern Med. 2005;165:2508-2513

# Smoking

# Depression

# Cardiovascular events

## Depression and Inflammation in Patient Coronary Heart Disease: Findings from the Heart and Soul Study

Mary A. Whooley, Catherine M. Caska, Bethany E. Hendrickson, Meghan A. and Sadia Ali

**Background:** Depression and inflammation independently predict adverse cardiovascular outcomes (CHD). Depression has been associated with elevated levels of inflammation in otherwise healthy patients. We investigated the link between depression and inflammation in patients with established CHD using blood samples for measurement of five inflammatory biomarkers (white blood cell count, CD40 ligand, and interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of markers, adjusted for potential confounding variables.

**Methods:** We sought to examine the association of major depression with inflammation in 984 outpatients with coronary heart disease. We assessed current major depression with the Computerized Diagnostic Interview Schedule (DISC) and measured five inflammatory biomarkers (white blood cell count, CD40 ligand, and interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of markers, adjusted for potential confounding variables.

**Results:** Of the 984 participants, 217 (22%) had current major depression. Depression was not an independent inflammatory marker. Contrary to our hypothesis, depression was associated with lower levels of CRP ( $p = .007$ ) in both unadjusted and adjusted models.

**Conclusions:** We found no evidence that current depression is associated with greater inflammation in outpatients with CHD. Inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with established CHD.

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Mary A. Whooley, M.D.

**Objective:** Depressive symptoms are associated with an increased risk of cardiac events in patients with heart disease. Elevated catecholamine levels may contribute to this association, but whether depressive symptoms are associated with catecholamine levels in patients with heart disease is unknown.

**Method:** The authors examined the association between depressive symptoms (defined by a Patient Health Questionnaire score  $\geq 10$ ) and 24-hour urinary norepinephrine, epinephrine, and dopamine excretion levels in 598 subjects with coronary disease.

**Results:** Depressive symptoms were more likely than those without depressive symptoms to have norepinephrine excretion levels in the highest quartile and above the normal range. Depressive symptoms were not associated with epinephrine or dopamine excretion levels.

**Conclusions:** In patients with coronary disease, depressive symptoms are associated with elevated levels of norepinephrine excretion.

## Depression and 24-Hour Urinary Cortisol Outpatients with Coronary Heart Disease and Soul Study

Christian Otte, Charles R. Marmar, Sharon S. Pipkin, Rudolf Moos, Warren S. Browner, M.D., M.P.H., Mary A. Whooley

**Background:** In patients with coronary heart disease (CHD), depression leads to worse cardiovascular outcomes. Elevated cortisol levels are associated with increased risk of cardiovascular events. However, it is not known whether depression is associated with elevated cortisol levels in patients with CHD.

**Methods:** We examined the association between depression (assessed by the Computerized Diagnostic Interview Schedule) and 24-hour urinary cortisol in 695 medical outpatients with known CHD.

**Results:** Of 695 participants, 138 (20%) had current depression. Depressed participants had higher 24-hour urinary cortisol levels ( $42 \pm 25$  vs.  $35 \pm 20$   $\mu\text{g/day}$ ,  $p < .01$ ). With each increasing quartile of cortisol concentration, the frequency of depression increased ( $p < .01$ ). Participants in the highest quartile of cortisol had a twofold increased odds of having depression, compared with those in the lowest quartile (odds ratio [OR] 2.1, 95% confidence interval [CI] 1.2-3.6,  $p = .01$ ). This association remained significant after adjusting for age, sex, body mass index, smoking, medication use, and cardiac function.

## Depression and Heart Rate Variability in Patients With Stable Coronary Heart Disease

Findings From the Heart and Soul Study

Anil Gehi, MD; Dennis Mangano, PhD, MD; Sharon Pipkin, MPH; Warren S. Browner, MD, MPH; Mary A. Whooley, MD

**Context:** Depression is associated with low heart rate variability (HRV) in patients following myocardial infarction, suggesting that alterations in the autonomic nervous system may contribute to the adverse cardiac outcomes associated with depression. Whether depression is associated with low HRV in patients with stable coronary heart disease (CHD) is not known.

**Objective:** To examine the association between major depression and 24-hour HRV in patients with stable CHD.

**Design, Setting, and Participants:** Cross-sectional study of 873 outpatients with stable CHD recruited from outpatient clinics in the San Francisco Bay Area, California.

**Main Outcome Measures:** Major depression was assessed using the Computerized National Institute of Mental Health Diagnostic Interview Schedule. Heart rate variability was measured using 24-hour ambulatory electrocardiography.

**Results:** A total of 195 depressed patients were included in the analysis. Depression was associated with lower 24-hour HRV ( $p < .01$ ). This association remained significant after adjusting for age, sex, body mass index, smoking, medication use, and cardiac function.

**Conclusions:** We found that depression is associated with lower 24-hour HRV in patients with stable CHD. These findings suggest that depression may contribute to the adverse cardiac outcomes associated with depression in patients with stable CHD.

**Arch Gen Psychiatry.** 2004;61:1179-1184.

## Association of a Serotonin Transporter Polymorphism (5-HTTLPR) With Depression, Perceived Stress, and Norepinephrine in Patients With Coronary Disease: The Heart and Soul Study

Christian Otte, M.D.  
Jeanne McCaffery, Ph.D.  
Sadia Ali, M.P.H.  
Mary A. Whooley, M.D.

**Objective:** The short allele of a functional polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) has been shown to interact with stressful life events to predict depression in otherwise healthy individuals. Whether the short allele increases risk for depression associated with the stress of a chronic illness has not been established.

**Method:** In a cross-sectional genetic association study, the authors examined the association of 5-HTTLPR with current depression (measured by the Computerized Diagnostic Interview Schedule), perceived stress (measured by the Perceived Stress Scale), and 24-hour urinary norepinephrine excretion in 557 outpatients with chronic coronary disease.

**Results:** Among individuals carrying an s allele, 25% (97 of 383) had current depression, compared with 17% (29 of 174) of ll homozygotes. The unadjusted odds ratio was 1.6, with a 95% confidence interval (CI) of 1.0-2.6; the age- and gender-adjusted odds ratio was also 1.6 (95% CI = 1.0-2.5). Participants carrying an s allele had a higher mean score for perceived stress than ll homozygotes (5.4 versus 4.7) and a higher rate of moderate or high perceived stress (adjusted odds ratio = 1.6, 95% CI = 1.1-2.3). Mean 24-hour norepinephrine excretion was higher in s allele carriers (55.6 versus 50.2  $\mu\text{g/day}$ ), who were more likely to have norepinephrine values in the highest quartile (adjusted odds ratio = 1.7, 95% CI = 1.0-3.0).

**Conclusions:** Among patients with chronic illness, carriers of the s allele of 5-HTTLPR are more vulnerable to depression, perceived stress, and high norepinephrine secretion. These factors may contribute to worse cardiovascular outcomes in these patients.

[Am J Psychiatry 2007; 164:1379-1384]

## Relation Between Depressive Symptoms and Treadmill Exercise Capacity in the Heart and Soul Study

Bernice Ruo, MD, John S. Rumsfeld, MD, PhD, Sharon Pipkin, MPH, and Mary A. Whooley, MD

To examine the association between depressive symptoms and exercise capacity, we performed a cross-sectional study of 944 outpatients with stable coronary artery disease and found that the presence of depressive symptoms was independently associated with poor exercise capacity ( $< 5$  MET tasks achieved; adjusted odds ratio 1.8, 95% confidence interval 1.1 to 2.7,  $p = 0.01$ ). Depressive symptoms should be considered in the differential diagnosis of poor exercise capacity. ©2004 by Excerpta Medica, Inc.

[Am J Cardiol 2004;94:96-99]

Our goal in this study was to examine the relation between depressive symptoms and treadmill exercise capacity in 944 patients with stable coronary artery disease (CAD). We hypothesized that depressive symptoms would be associated with lower exercise capacity. We found that the presence of depressive symptoms was independently associated with lower exercise capacity. This association remained significant after adjusting for age, sex, body mass index, smoking, medication use, and cardiac function.

Each participant underwent a symptom-limited exercise treadmill test according to the Bruce protocol. To achieve maximum heart rate, participants who were unable to continue the Bruce protocol (for orthopedic or other reasons) were switched to slower settings on the treadmill and encouraged to exercise for as long as possible. Exercise capacity was calculated as the total number of METs achieved. Beforehand, we categorized participants into those with poor ( $< 5$  METs) and normal ( $\geq 5$  METs) exercise capacity. To calculate percent maximum heart rate achieved, the maximum heart rate achieved was divided by  $(220 - \text{age})$ .

## Depression and Medication Adherence in Outpatients With Coronary Heart Disease

Findings From the Heart and Soul Study

Anil Gehi, MD; Donald Haas, MD, MPH; Sharon Pipkin, MPH; Mary A. Whooley, MD

**Background:** Depression leads to adverse outcomes in patients with coronary heart disease (CHD). Medication nonadherence is a potential mechanism for the increased risk of CHD events associated with depression, but it is not known whether depression is associated with medication nonadherence in outpatients with stable CHD.

**Methods:** We examined the association between current major depression (assessed using the Diagnostic Interview Schedule) and self-reported medication adherence in a cross-sectional study of 940 outpatients with stable CHD.

**Results:** A total of 204 participants (22%) had major depression. Twenty-eight (14%) of 204 depressed participants reported not taking their medications as prescribed compared with 40 (3%) of 736 nondepressed participants (odds ratio [OR] 2.8, 95% confidence interval [CI] 1.7-4.7,  $P < .001$ ). Twice as many depressed participants as nondepressed participants reported not taking their medications as prescribed.

**Conclusions:** Depression is associated with medication nonadherence in outpatients with stable CHD. This association remained significant after adjusting for age, sex, body mass index, smoking, medication use, and cardiac function.

**Arch Intern Med.** 2004;164:1179-1184.

## Depressive Symptoms, Health Behaviors, and Risk of Cardiovascular Events in Patients With Coronary Heart Disease

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Christian Otte, MD  
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Mitchell D. Feldman, MD, MPhil  
Nelson B. Schiller, MD  
Warren S. Browner, MD, MPH

**Context:** Depressive symptoms predict adverse cardiovascular outcomes in patients with coronary heart disease, but the mechanisms responsible for this association are unknown.

**Objective:** To determine why depressive symptoms are associated with an increased risk of cardiovascular events.

**Design and Participants:** The Heart and Soul Study is a prospective cohort study of 1017 outpatients with stable coronary heart disease followed up for a mean (SD) of 4.8 (1.4) years.

**Setting:** Participants were recruited between September 11, 2000, and December 20, 2002, from 12 outpatient clinics in the San Francisco Bay Area and were followed up to January 12, 2008.

**Main Outcome Measures:** Baseline depressive symptoms were assessed using the Patient Health Questionnaire (PHQ). We used proportional hazards models to evaluate the extent to which the association of depressive symptoms with subsequent cardiovascular events (heart failure, myocardial infarction, stroke, transient ischemic attack, or death) was explained by baseline disease severity and potential biological or behavioral mediators.

### Article

## Association of a Serotonin Transporter Polymorphism (5-HTTLPR) With Depression, Perceived Stress, and Norepinephrine in Patients With Coronary Disease: The Heart and Soul Study

Christian Otte, M.D.  
Jeanne McCaffery, Ph.D.  
Sadia Ali, M.P.H.  
Mary A. Whooley, M.D.

**Objective:** The short allele of a functional polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) has been shown to interact with stressful life events to predict depression in otherwise healthy individuals. Whether the short allele increases risk for depression associated with the stress of a chronic illness has not been established.

**Method:** In a cross-sectional genetic association study, the authors examined the association of 5-HTTLPR with current depression (measured by the Computerized Diagnostic Interview Schedule), perceived stress (measured by the Perceived Stress Scale), and 24-hour urinary norepinephrine excretion in 557 outpatients with chronic coronary disease.

**Results:** Among individuals carrying an s allele, 25% (97 of 383) had current depression, compared with 17% (29 of 174) of ll homozygotes. The unadjusted odds ratio was 1.6, with a 95% confidence interval (CI) of 1.0-2.6; the age- and gender-adjusted odds ratio was also 1.6 (95% CI = 1.0-2.5). Participants carrying an s allele had a higher mean score for perceived stress than ll homozygotes (5.4 versus 4.7) and a higher rate of moderate or high perceived stress (adjusted odds ratio = 1.6, 95% CI = 1.1-2.3). Mean 24-hour norepinephrine excretion was higher in s allele carriers (55.6 versus 50.2  $\mu\text{g/day}$ ), who were more likely to have norepinephrine values in the highest quartile (adjusted odds ratio = 1.7, 95% CI = 1.0-3.0).

**Conclusions:** Among patients with chronic illness, carriers of the s allele of 5-HTTLPR are more vulnerable to depression, perceived stress, and high norepinephrine secretion. These factors may contribute to worse cardiovascular outcomes in these patients.

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outpatients with stable coronary heart disease: a cross-sectional study

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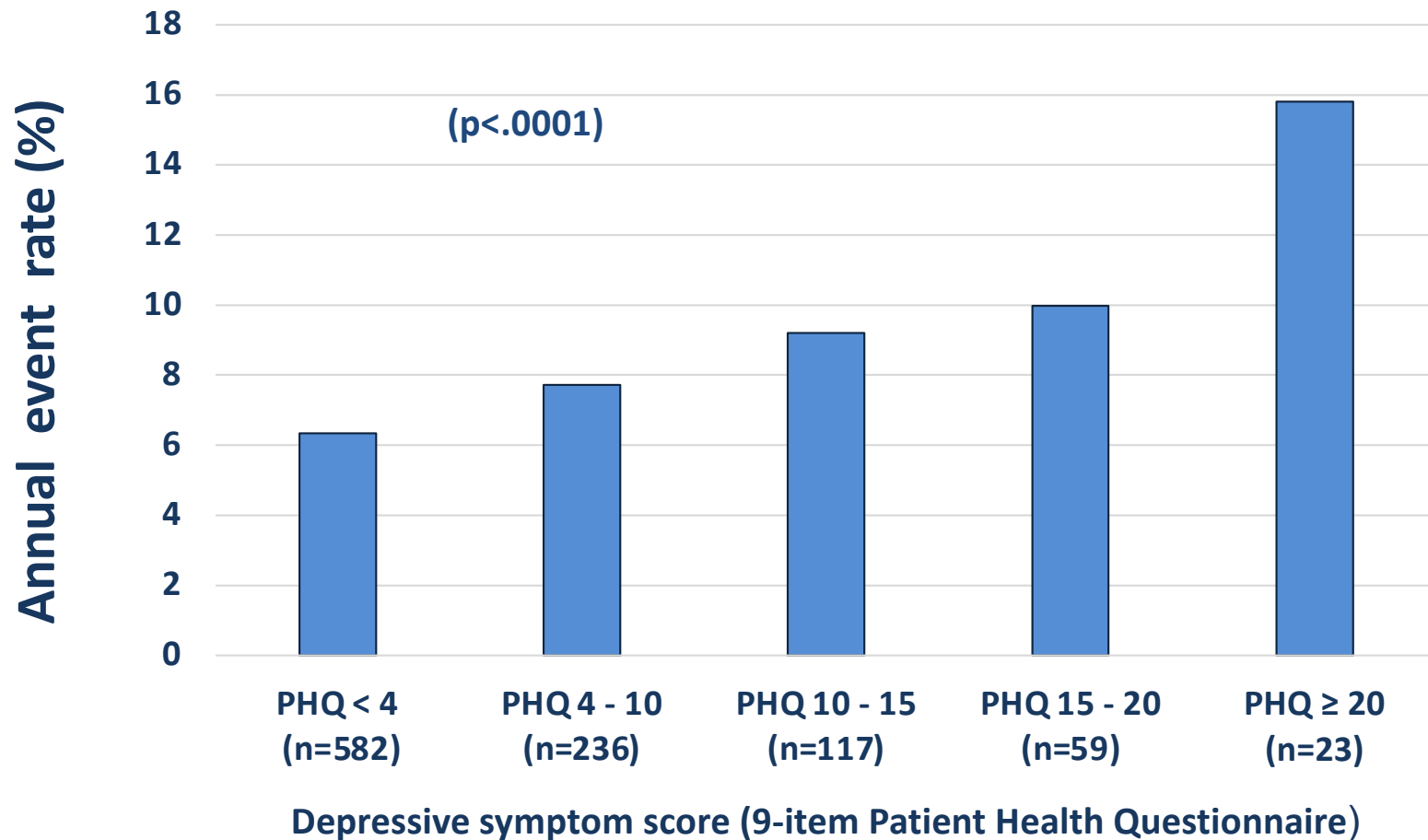
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<sup>g</sup>Department of Psychiatry, University of California, San Francisco, CA, United States

## Annual rate of recurrent cardiovascular events (MI, CHF, stroke, or death) during 5-year follow up in 1017 patients



**Association between depressive symptoms  
(PHQ-9 score  $\geq 10$  vs.  $< 10$ ) and CV events**

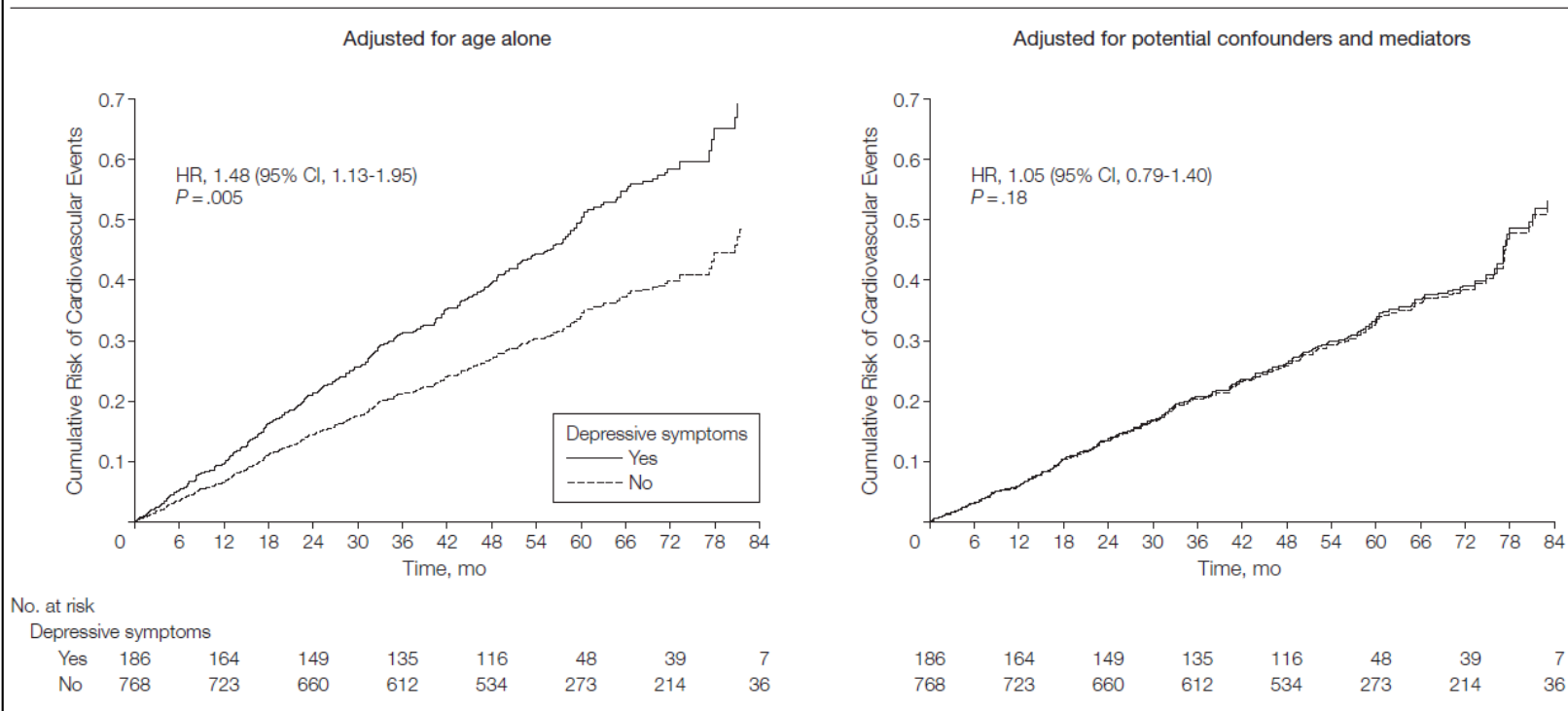
<i>Covariates adjusted for</i>	<i>Excess risk associated with depressive symptoms</i>
Age	50%

## Association between depressive symptoms (PHQ-9 score $\geq 10$ vs. $< 10$ ) and CV events

<i>Covariates adjusted for</i>	<i>Excess risk associated with depressive symptoms</i>
Age	50%
Add education, prior MI, DM, CHF, LV ejection fraction	31%
Add log CRP	24%
Add smoking	20%
Add medication non-adherence	18%
Add physical inactivity	5%

# Poor health behaviors (especially physical inactivity) responsible for excess risk of cardiovascular events

**Figure 1.** Cumulative Risk of Cardiovascular Events



Data are stratified by depressive symptoms before and after adjustment for health behaviors in 954 participants with complete data. The adjusted hazard ratio (HR) differs slightly from Table 4 because 63 patients with incomplete data were excluded from the analysis. CI indicates confidence interval.

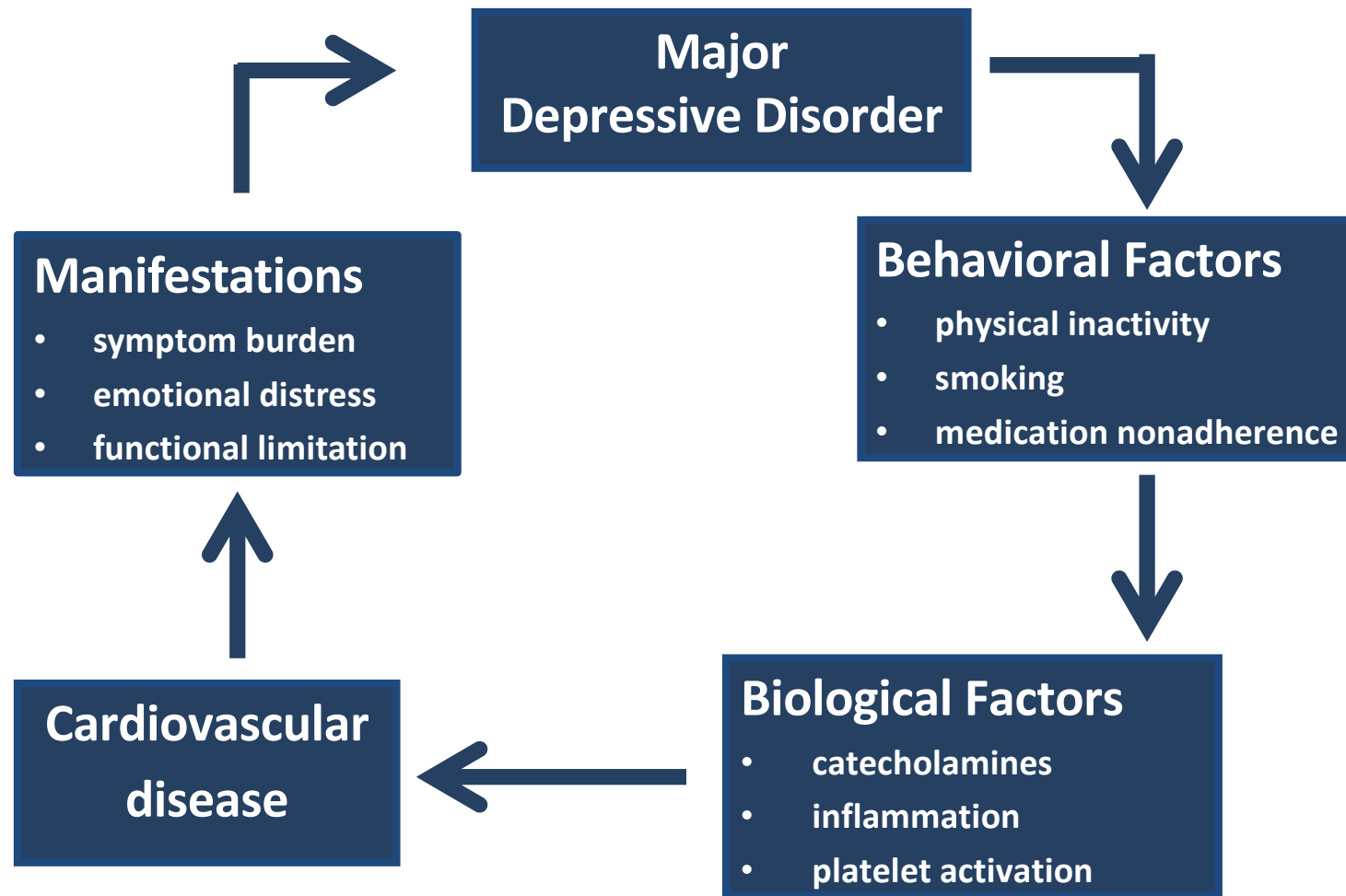
JAMA. 2008;300:2379-2388. <https://doi.org/10.1001/jama.2008.711>

# Depressive Symptoms, Health Behaviors, and Risk of Cardiovascular Events in Patients With Coronary Heart Disease

**Conclusion** In this sample of outpatients with coronary heart disease, the association between depressive symptoms and adverse cardiovascular events was largely explained by behavioral factors, particularly physical inactivity.

*JAMA. 2008;300(20):2379-2388*

[www.jama.com](http://www.jama.com)





# Heart and Soul and Cardiac Rehabilitation



- Depression associated with adverse cardiovascular outcomes
- Key role of health behaviors (especially physical inactivity)
- **Cardiac rehabilitation an underutilized opportunity to treat both**
- **Ways to improve engagement in cardiac rehabilitation**
- **Potential benefits of COVID pandemic on cardiac rehab delivery**

Guideline

> Clin Pract Guidel Quick Ref Guide Clin 1995 Oct;(17):1-23.

# **Cardiac rehabilitation as secondary prevention. Agency for Health Care Policy and Research and National Heart, Lung, and Blood Institute**

N K Wenger, E S Froelicher, L K Smith, P A Ades, K Berra, J A Blumenthal, C M Certo, A M Dattilo, D Davis, R F DeBusk, et al.

PMID: 8595435

## EFFECTS OF EXERCISE AND CARDIAC REHABILITATION ON CARDIOVASCULAR OUTCOMES

Philip A. Ades, MD, and Cesar E. Coello, MD

The introduction of physical exercise to the treatment of patients with coronary heart disease (CHD) was initially based on an intent to avoid the deconditioning, medical complications, and disability that result from prolonged bed rest and limited outpatient physical activity.<sup>17, 63</sup> Outpatient exercise programs were initially limited to low-risk coronary patients but evolved to incorporate additional risk reduction interventions for a broader patient population.<sup>63</sup>

*Medical Clinics of North America, 2000*

Review Article

*Medical Progress*

**CARDIAC REHABILITATION AND  
SECONDARY PREVENTION OF  
CORONARY HEART DISEASE**

PHILIP A. ADES, M.D.

**C**ORONARY heart disease is the leading cause of death in the United States among men and women.<sup>1</sup> It is also a major cause of physical disability, particularly in the rapidly growing population of elderly persons.<sup>2,3</sup> In 1997, acute myocardial infarction was diagnosed in 1.1 million Americans, and 800,000 patients underwent coronary revascularization.<sup>1</sup> The prevention of subsequent coronary events and the maintenance of physical functioning in such patients are major challenges in preventive care.

Cardiac-rehabilitation programs were first developed in the 1960s,<sup>4-6</sup> once the benefits of ambulation during prolonged hospitalization for coronary events had been recognized.<sup>7</sup> After discharge from the hospital, the process of physical reconditioning was continued at home. Concern about the safety of unsupervised exercise after discharge led to the development of highly

ary prevention are broad and compelling. Controlled trials of exercise after myocardial infarction, reported in the 1980s, have demonstrated reductions in overall mortality and in mortality from cardiovascular causes.<sup>9,10</sup> Trials of exercise combined with nutritional counseling have demonstrated a slowing of the atherosclerotic process<sup>12,13,15,16</sup> and decreased rates of subsequent coronary events and hospitalization.<sup>11,13</sup> Despite the well-established benefits of exercise and nutritional counseling, physicians are generally not well trained, and do not have the time to provide effective nutritional advice, guidance about weight management, and a prescription for exercise. The provision of all these services at cardiac-rehabilitation centers, with the use of well-established algorithms to set goals for risk reduction<sup>17,18</sup> and in coordination with the primary care physician, is efficient and effective.

Only 10 to 20 percent of appropriate candidates in the United States currently participate in formal rehabilitation programs.<sup>14,19</sup> The reasons for low participation rates include the geographic maldistribution of available programs and the failure of physicians to refer patients, particularly elderly persons and women, to the programs.<sup>20,21</sup> Home-base rehabilitation programs that are directed by physicians and coordinated by nurses have been developed as a way of expanding the delivery of secondary-prevention services.<sup>13,22,23</sup>

# Exercise-Based Cardiac Rehabilitation for Coronary Heart Disease

## Cochrane Systematic Review and Meta-Analysis

Lindsey Anderson, PhD,\* Neil Oldridge, PhD,† David R. Thompson, PhD,‡ Ann-Dorthe Zwisler, MD,§  
Karen Rees, PhD,|| Nicole Martin, MA,¶ Rod S. Taylor, PhD\*



### ABSTRACT

**BACKGROUND** Although recommended in guidelines for the management of coronary heart disease (CHD), concerns have been raised about the applicability of evidence from existing meta-analyses of exercise-based cardiac rehabilitation (CR).

**OBJECTIVES** The goal of this study is to update the Cochrane systematic review and meta-analysis of exercise-based CR for CHD.

**METHODS** The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, and Science Citation Index Expanded were searched to July 2014. Retrieved papers, systematic reviews, and trial registries were hand-searched. We included randomized controlled trials with at least 6 months of follow-up, comparing CR to no-exercise controls following myocardial infarction or revascularization, or with a diagnosis of angina pectoris or CHD defined by angiography. Two authors screened titles for inclusion, extracted data, and assessed risk of bias. Studies were pooled using random effects meta-analysis, and stratified analyses were undertaken to examine potential treatment effect modifiers.

**RESULTS** A total of 63 studies with 14,486 participants with median follow-up of 12 months were included. Overall, CR led to a reduction in cardiovascular mortality (relative risk: 0.74; 95% confidence interval: 0.64 to 0.86) and the risk of hospital admissions (relative risk: 0.82; 95% confidence interval: 0.70 to 0.96). There was no significant effect on total mortality, myocardial infarction, or revascularization. The majority of studies (14 of 20) showed higher levels of health-related quality of life in 1 or more domains following exercise-based CR compared with control subjects.

**CONCLUSIONS** This study confirms that exercise-based CR reduces cardiovascular mortality and provides important data showing reductions in hospital admissions and improvements in quality of life. These benefits appear to be consistent across patients and intervention types and were independent of study quality, setting, and publication date.

(J Am Coll Cardiol 2016;67:1-12) © 2016 by the American College of Cardiology Foundation.

- Cardiac rehab leads to 26% reduction in 12-month mortality after MI or revascularization

# Effect of exercise-based cardiac rehabilitation on anxiety and depression in patients with myocardial infarction: A systematic review and meta-analysis



Xianghui Zheng<sup>a,b</sup>, Yang Zheng<sup>a,b</sup>, Jing Ma<sup>c</sup>, Maomao Zhang<sup>a,b</sup>, Yongxiang Zhang<sup>a,b</sup>, Xianglan Liu<sup>a,b</sup>, Liangqi Chen<sup>a,b</sup>, Qingyuan Yang<sup>a,b</sup>, Yong Sun<sup>a,b</sup>, Jian Wu<sup>a,b\*</sup>, Bo Yu<sup>a,b</sup>

<sup>a</sup> Department of Cardiology, the Second Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang Province, China

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<sup>c</sup> Department of Cardiology, Chinese PLA General Hospital, Beijing, China

## ARTICLE INFO

### Article history:

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Available online 23 October 2018

### Keywords:

Cardiac rehabilitation

Anxiety

Depression

Myocardial infarction

## ABSTRACT

**Background:** Cardiac rehabilitation (CR) has been shown to provide the best social, psychological and physical conditions for patient recovery after myocardial infarction (MI).

**Objectives:** The aim of present study was to quantify the efficacy of exercise-based CR treatments in terms of relief from symptoms of anxiety and depression symptoms among patients with MI.

**Methods:** Literature published up to August 2017 was reviewed systematically using relevant keywords, MeSH terms, and Emtree headings to search PubMed, Embase, CINAHL (Ebsco), Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science. The results of included studies were compared meta-analytically.

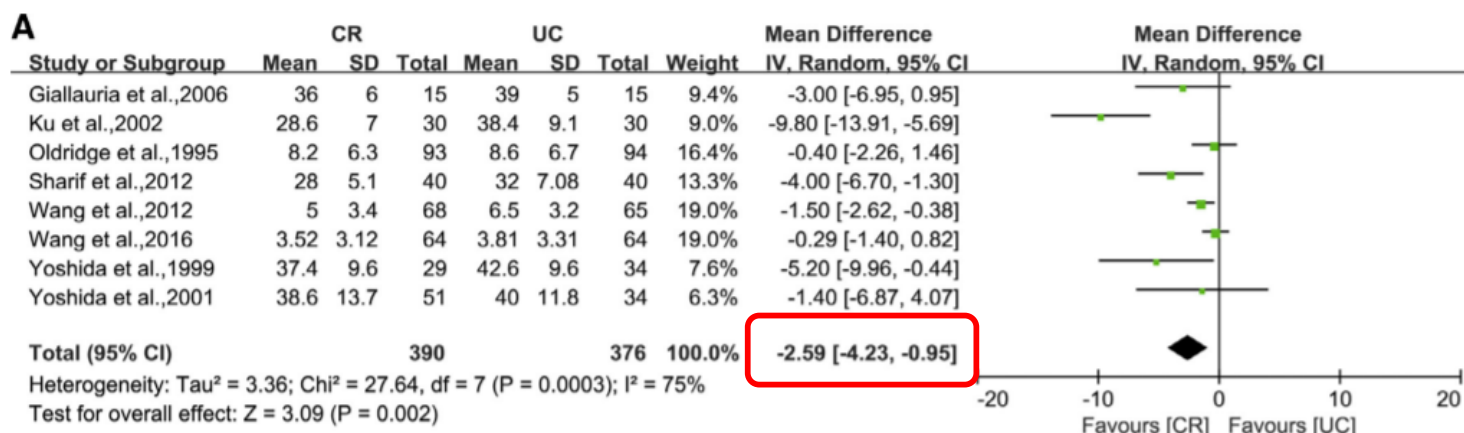
**Results:** We found that exercise-based CR had a significant effect on decreasing anxiety and depression scores. Furthermore, exercise-based CR may alleviate anxiety and depressive symptoms at different time periods.

**Conclusions:** For patients with MI, exercise-based CR has been demonstrated to alleviate anxiety and depressive symptoms. These findings highlight CR as essential and beneficial for minimizing MI patient anxiety and depression during recovery.

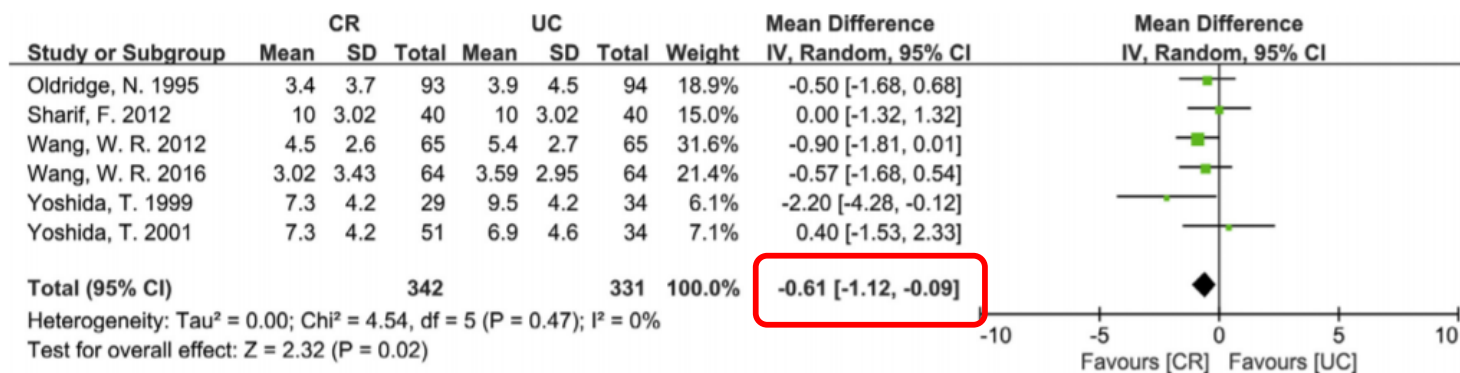
© 2018 Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.hrtlng.2018.09.011>

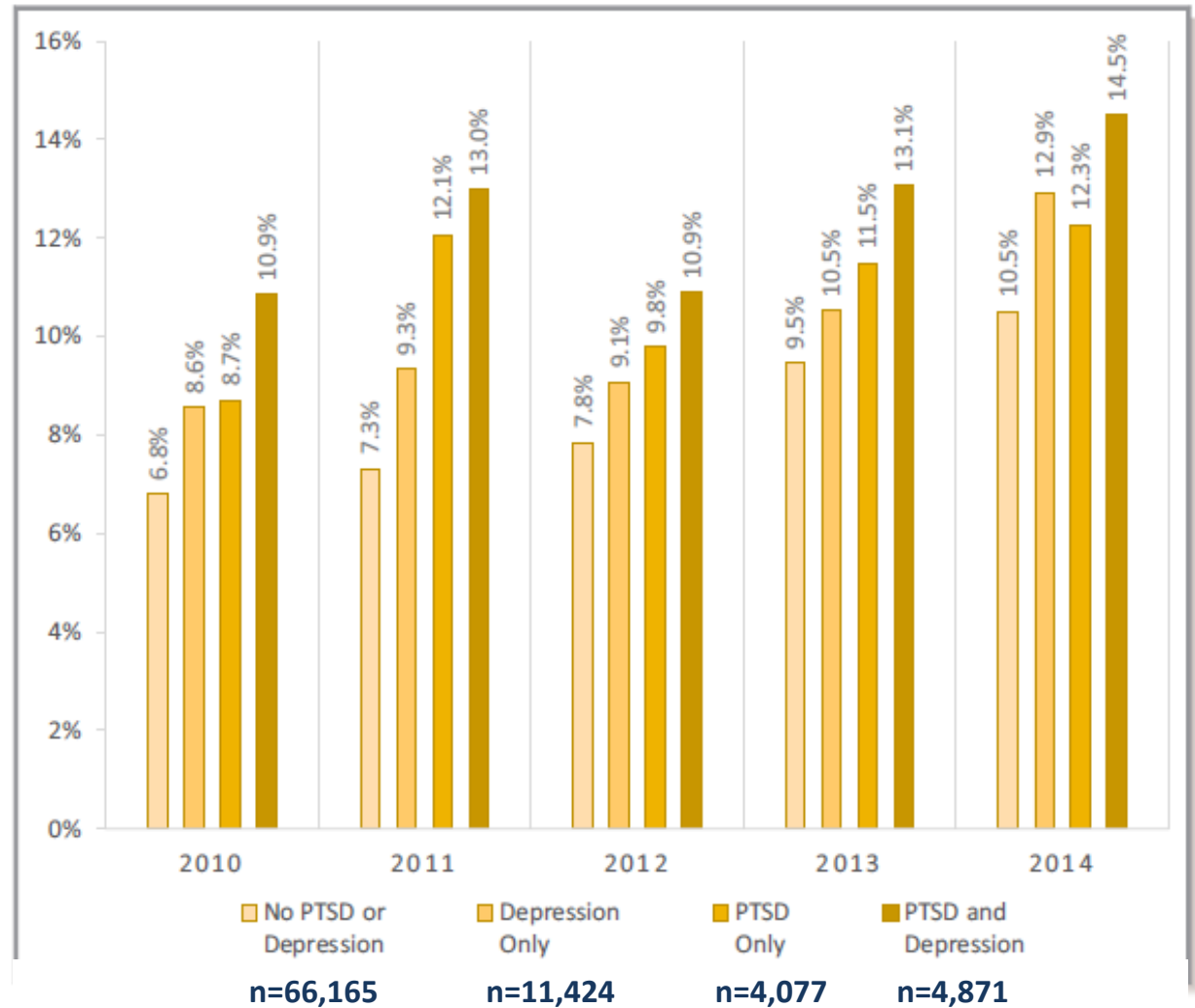
## Effects of exercise-based CR on anxiety



## Effects of exercise-based CR on depression



PTSD and depression associated with **higher** CR participation rates in 86,537 Veterans with ischemic heart disease



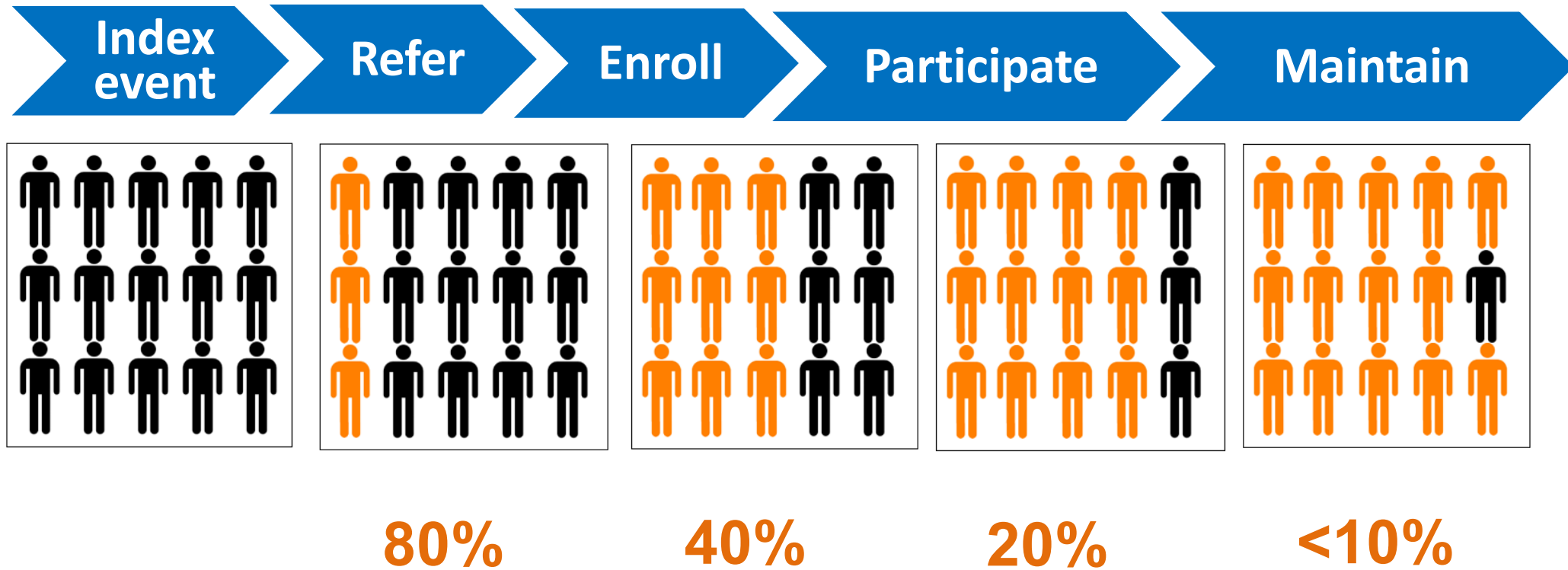
**Figure.** Adjusted cardiac rehabilitation participation rates by posttraumatic stress disorder (PTSD)/depression status and year.

Krishnamurthi et al,  
*J Am Heart Assoc.* 2019;8:e011639.  
 DOI: 10.1161/JAHA.118.011639.



# **Cardiac Rehabilitation Vastly Underutilized in U.S.**

# Cardiac Rehabilitation Vastly Underutilized in U.S.



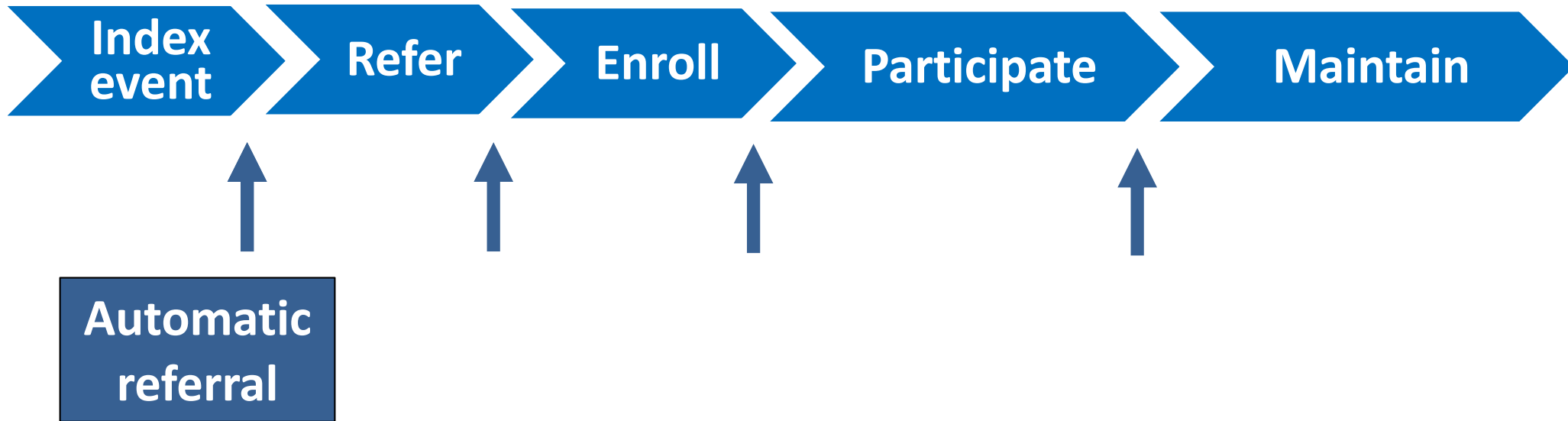


*Mayo Clinic Proceedings, 2017;92:234-242*

# Increasing Cardiac Rehabilitation Participation From 20% to 70%: A Road Map From the Million Hearts Cardiac Rehabilitation Collaborative

Philip A. Ades, MD; Steven J. Keteyian, PhD; Janet S. Wright, MD;  
Larry F. Hamm, PhD; Karen Lui, RN, MS; Kimberly Newlin, ANP;  
Donald S. Shepard, PhD; and Randal J. Thomas, MD, MS

# Quality Gaps = Opportunities for Improvement



*Journal of Cardiopulmonary Rehabilitation and Prevention, 2009*

## Effect of a Computerized Referral at Hospital Discharge on Cardiac Rehabilitation Participation Rates

Enkhtuyaa Mueller, MD, Patrick D. Savage, MS, David J. Schneider, MD, Laura L. Howland, RN, and Philip A. Ades, MD

**→ Automated referral (embedded in discharge summary) improved participation in >800 patients with MI or CABG**



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**CANADIAN ASSOCIATION OF CARDIAC REHABILITATION (CACR) –  
CANADIAN CARDIOVASCULAR SOCIETY POSITION STATEMENT (CCS)**

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**Systematizing Inpatient Referral to Cardiac Rehabilitation: A joint policy position of  
the Canadian Association of Cardiac Rehabilitation and  
Canadian Cardiovascular Society**

*Endorsed by the Cardiac Care Network of Ontario*

Printed in *CJC* 2011;27:192-199 and online *JCRP*, March/April 2011 Vol. 31, Issue 2.

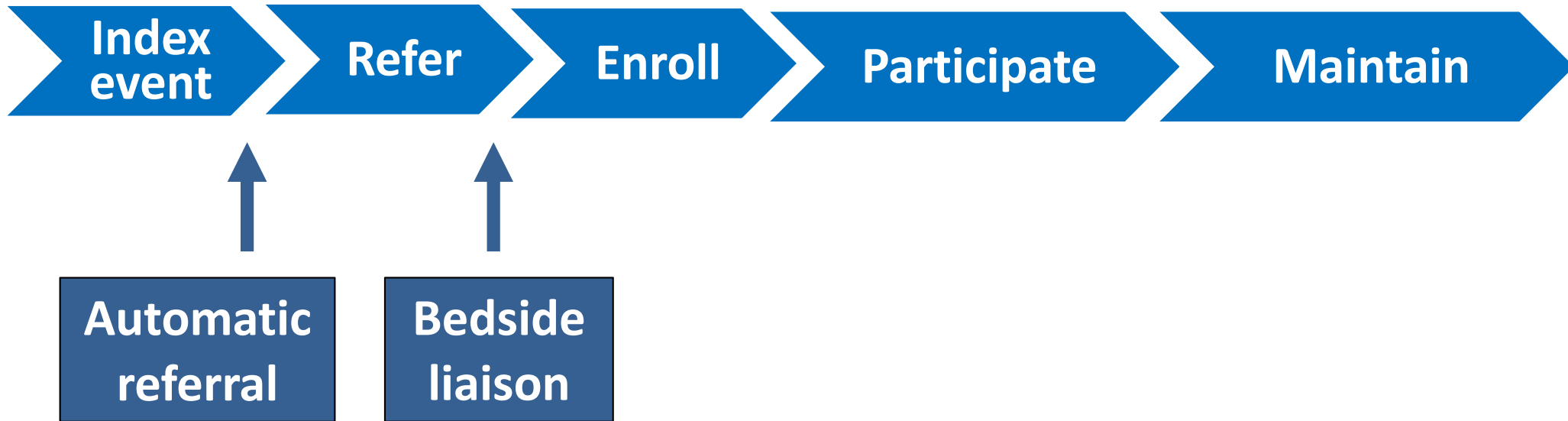
Sherry L. Grace, PhD (chair) & Caroline Chessex, MD, FRCPC (co-Chair)

Primary Panel Writing Group: Heather Arthur, Sammy Chan, Cleo Cyr, William Dafoe,  
Martin Juneau, Paul Oh, Neville Suskin.

Secondary Panel Writing Group: Paul Poirier, Rob Stevenson, Jim Stone.

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# Quality Gaps = Opportunities for Improvement

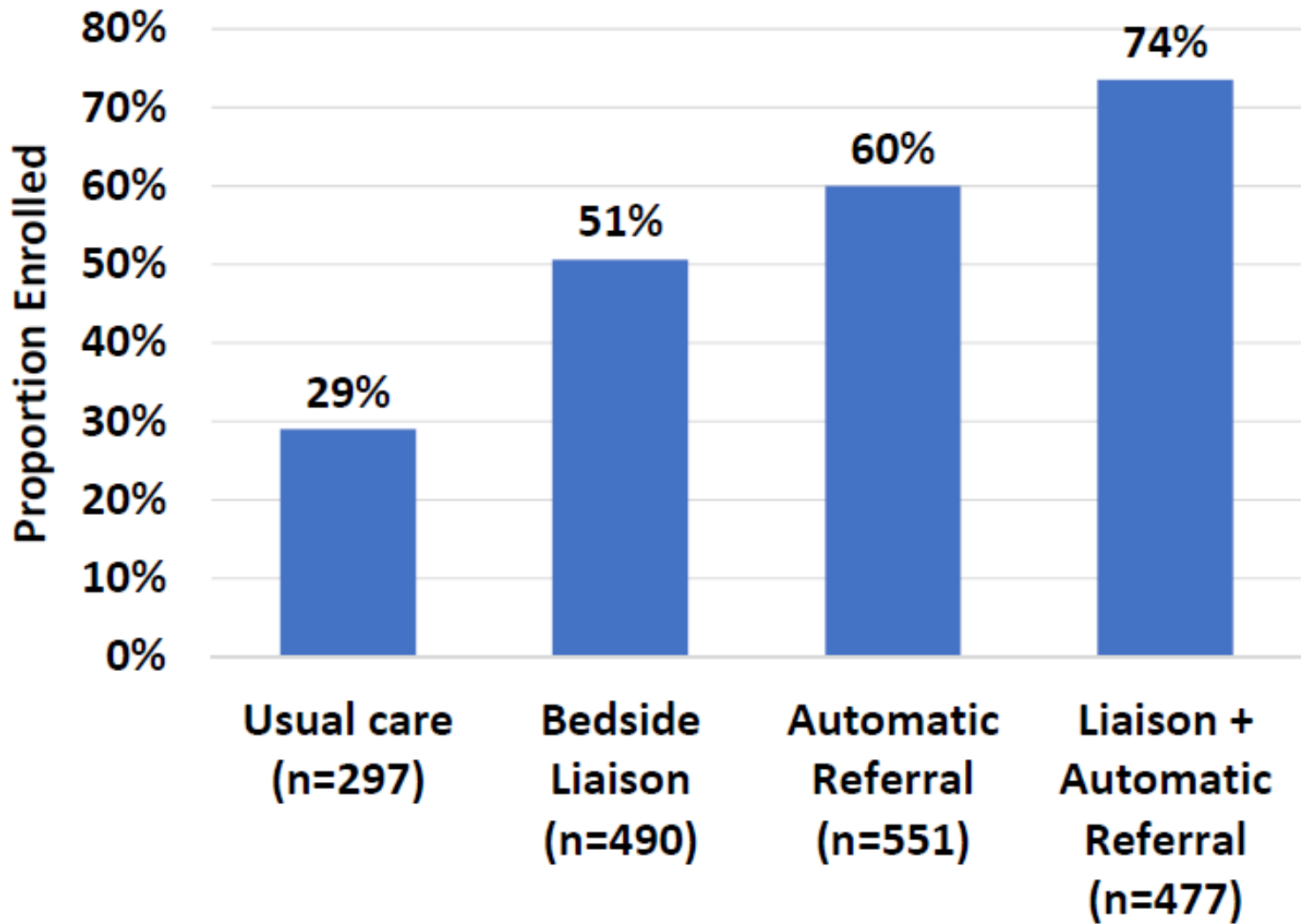


After a heart attack, stent placement, or bypass surgery, patients feel highly motivated to make lifestyle changes.



This is a huge opportunity to improve health and longevity.





*Grace et al, 2011*  
*Arch Int Med*

# Effect of Cardiac Rehabilitation Referral Strategies on Utilization Rates

## *A Prospective, Controlled Study*

Sherry L. Grace, PhD; Kelly L. Russell, MSc; Robert D. Reid, PhD, MBA; Paul Oh, MD, FRCPC; Sonia Anand, MD, PhD, FRCPC; James Rush, PhD; Karen Williamson, PhD; Milan Gupta, MD; David A. Alter, MD, PhD, FRCPC; Donna E. Stewart, MD, FRCPC; for the Cardiac Rehabilitation Care Continuity Through Automatic Referral Evaluation (CRCARE) Investigators

**Background:** Although cardiac rehabilitation (CR) has been shown to reduce mortality and is a recommended component in clinical practice guidelines, CR referral and utilization rates remain low. Referral strategies have been implemented to increase CR use but have yet to be compared concurrently. To determine the optimal strategy to maximize CR referral, enrollment, and participation, we evaluated 3 referral strategies compared with usual care: "automatic" only via discharge order or electronic record, health care provider liaison only, or a combined approach.

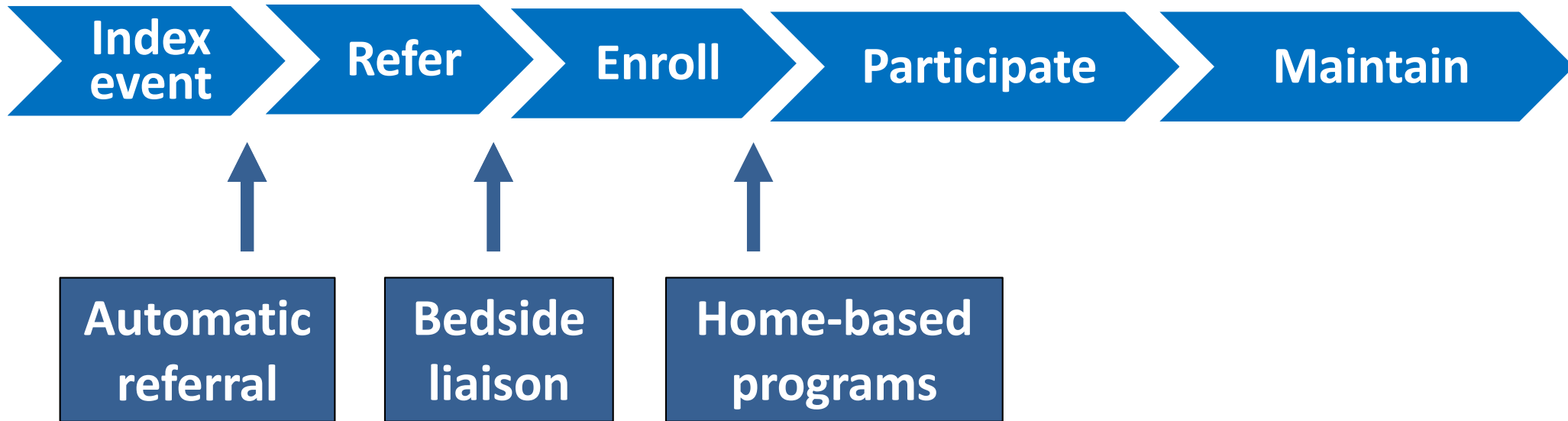
**Methods:** In this prospective controlled study, 2635 inpatients with coronary artery disease from 11 Ontario, Canada, hospitals using 1 of the 4 referral strategies completed a sociodemographic survey, and clinical data were extracted from medical charts. One year later, 1809 participants completed a mailed survey that assessed CR utilization. Referral strategies were compared using generalized estimating equations to control for effect of hospital.

**Results:** Adjusted analyses revealed referral strategy was significantly related to CR referral and enrollment ( $P < .001$ ). Combined automatic and liaison referral resulted in the greatest CR use (odds ratio [OR], 8.41; 85.8% referral, 73.5% enrollment), followed by automatic only (OR, 3.27; 70.2% referral, 60.0% enrollment), and liaison only (OR, 3.35; 59.0% referral, 50.6% enrollment), compared with usual referral (32.2% referral, 29.0% enrollment). The degree of CR participation did not differ by referral strategy among referred participants (mean [SD] percentage of classes attended, 82.87% [27.20%];  $P = .88$ ).

**Conclusions:** Automatic referral combined with a patient discussion can achieve among the highest rates of CR referral reported. Wider adoption of such strategies could ensure that 45% more patients being treated for cardiac disease would have access to and realize the benefits of CR.

*Arch Intern Med.* 2011;171(3):235-241

# Quality Gaps = Opportunities for Improvement



# A controlled trial of cardiac rehabilitation in the home setting using electrocardiographic and voice transtelephonic monitoring

Philip A. Ades, MD, Fredric J. Pashkow, MD, Gerald Fletcher, MD, Ileana L. Pina, MD, Lenore R. Zohman, MD, James R. Nestor, PhD *Burlington, Vt*

**Objective** The goal of this study was to compare the effectiveness of home-based, transtelephonically monitored cardiac rehabilitation with standard, on-site, supervised cardiac rehabilitation.

**Background** Participation in cardiac rehabilitation has been demonstrated to increase exercise capacity, decrease cardiovascular symptoms, improve psychosocial status, and decrease total and cardiovascular mortality rates in patients with coronary heart disease. Because of multiple factors, national overall participation is only at 15% of eligible patients.

**Methods** Effects of a 3-month home-based, transtelephonically monitored rehabilitation program (n = 83 patients) with simultaneous voice and electrocardiographic transmission to a centrally located nurse coordinator were compared with effects of a standard on-site rehabilitation program (n = 50 patients). The study design was a multicenter, controlled trial. Primary outcome variables were peak aerobic capacity and quality of life, as measured by the Health Status Questionnaire.

**Results** Patients in the home-based monitoring program increased peak aerobic capacity to a similar degree as patients who exercised on site (18% vs 23%). Quality of life domains of physical functioning, social functioning, physical role limitations, emotional role limitations, bodily pain, and energy/fatigue improved similarly in both groups. There were no circulatory arrests or other major exercise-related medical events in either group. A total of 3100 hours of home exercise were transtelephonically monitored.

*Am Heart J, 2000*



**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

*Cochrane Database of  
Systematic Reviews*

*2017, Issue 6*

[www.cochranelibrary.com](http://www.cochranelibrary.com)

## Home-based versus centre-based cardiac rehabilitation (Review)

Anderson L, Sharp GA, Norton RJ, Dalal H, Dean SG, Jolly K, Cowie A, Zawada A, Taylor RS.

**23 randomized trials → home- and center-based  
cardiac rehabilitation equally effective for  
improving clinical and health-related quality of**

## Home-Based vs. Center-Based CR

Outcome (3 to 12 months)	# Studies	Total # Subjects	Risk Ratio	95% CI
Smoking	5	986	1.02	0.83 – 1.27
Mortality	11	1505	1.19	0.65 – 2.16
<b>Completion</b>	<b>22</b>	<b>2615</b>	<b>1.04</b>	<b>1.00 – 1.08</b>

**Veterans Health Administration**

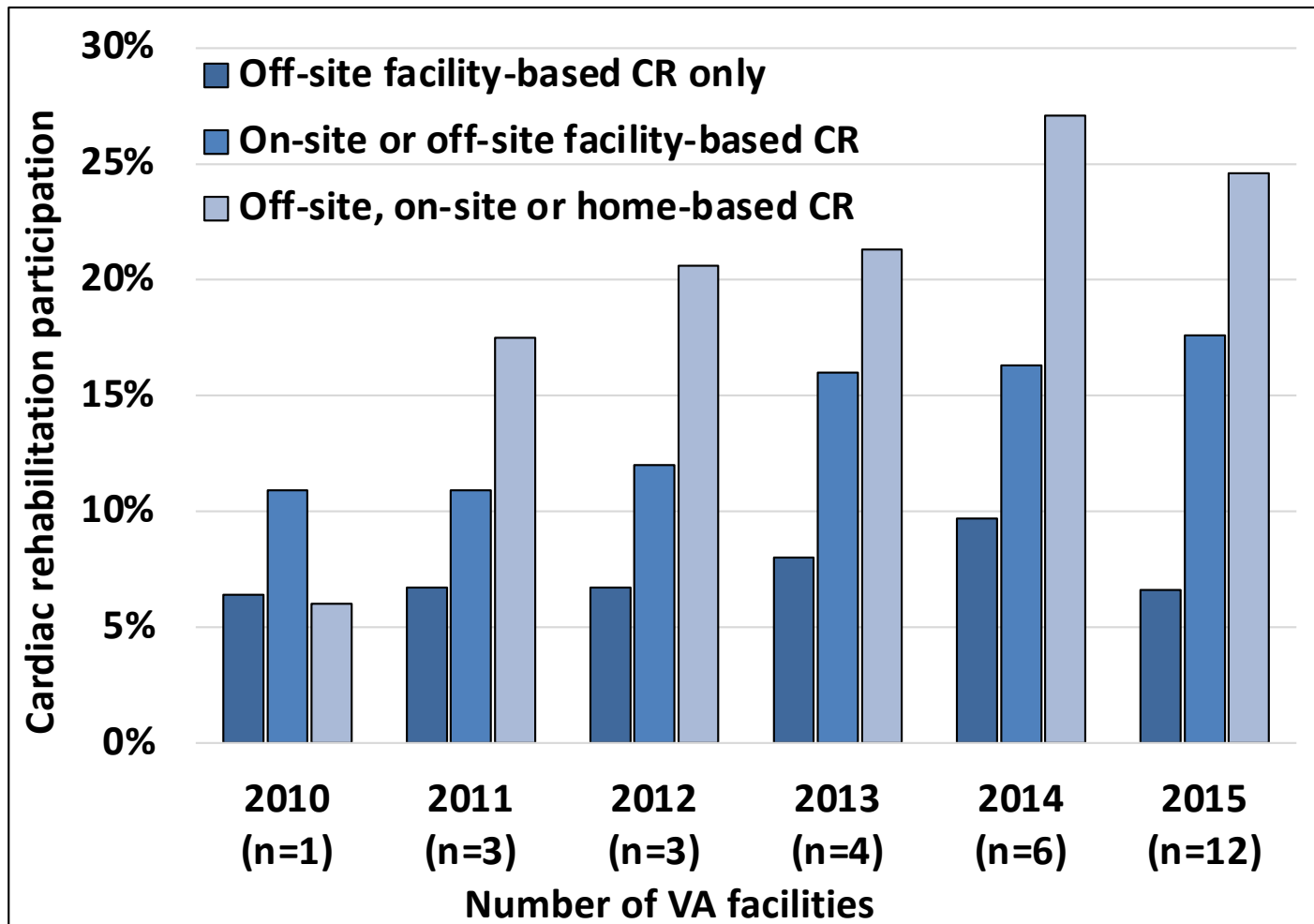
# The Design and Implementation of a Home-Based Cardiac Rehabilitation Program

Gregory Rohrbach, DNP; David W. Schopfer, MD; Nirupama Krishnamurthi, MBBS, MPH;  
Mark Pabst, MPH; Michael Bettencourt; Jo Loomis, DNP; Mary A. Whooley, MD

A home-based cardiac rehabilitation program improves access and enrollment by using  
an evidence-based alternative model of care.

<http://www.sanfrancisco.va.gov/services/HealthyHeart .asp>

## Availability of home-based CR → 4-fold greater participation



*Schopfer et al, JAMA-Int Med, 2018*



**Scientific  
Statement  
jointly  
published  
by 3 societies  
in 2019**

## **Home-Based Cardiac Rehabilitation**

**A Scientific Statement From the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Heart Association, and the American College of Cardiology**

**ABSTRACT:** Cardiac rehabilitation (CR) is an evidence-based intervention that uses patient education, health behavior modification, and exercise training to improve secondary prevention outcomes in patients with cardiovascular disease. CR programs reduce morbidity and mortality rates in adults with ischemic heart disease, heart failure, or cardiac surgery but are significantly underused, with only a minority of eligible patients participating in CR in the United States. New delivery strategies are urgently needed to improve participation. One potential strategy is home-based CR (HBCR). In contrast to center-based CR services, which are provided in a medically supervised facility, HBCR relies on remote coaching with indirect exercise supervision and is provided mostly or entirely outside of the traditional center-based setting. Although HBCR has been successfully deployed in the United Kingdom, Canada, and other countries, most US healthcare organizations have little to no experience with such programs. The purpose of this scientific statement is to identify the core components, efficacy, strengths, limitations, evidence gaps, and research necessary to guide the future delivery of HBCR in the United States. Previous randomized trials have generated low- to moderate-strength evidence that HBCR and center-based CR can achieve similar improvements in 3- to 12-month clinical outcomes. Although HBCR appears to hold promise in expanding the use of CR to eligible patients, additional research and demonstration projects are needed to clarify, strengthen, and extend the HBCR evidence base for key subgroups,

Randal J. Thomas, MD,  
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FACC, Chair  
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MAACVPR, FACC  
Theresa M. Beckie, PhD,  
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Steven J. Keteyian, PhD  
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Mary A. Whooley, MD,  
FAHA, FACC, Vice Chair

*Circulation.* 2019;140:e69–e89. DOI: 10.1161/CIR.0000000000000663

# The mobile revolution—using smartphone apps to prevent cardiovascular disease

*Lis Neubeck, Nicole Lowres, Emelia J. Benjamin, S. Ben Freedman, Genevieve Coorey and Julie Redfern*

**Abstract** | Cardiovascular disease (CVD) is the leading cause of morbidity and mortality globally. Mobile technology might enable increased access to effective prevention of CVDs. Given the high penetration of smartphones into groups with low socioeconomic status, health-related mobile applications might provide an opportunity to overcome traditional barriers to cardiac rehabilitation access. The huge increase in low-cost health-related apps that are not regulated by health-care policy makers raises three important areas of interest. Are apps developed according to evidenced-based guidelines or on any evidence at all? Is there any evidence that apps are of benefit to people with CVD? What are the components of apps that are likely to facilitate changes in behaviour and enable individuals to adhere to medical advice? In this Review, we assess the current literature and content of existing apps that target patients with CVD risk factors and that can facilitate behaviour change. We present an overview of the current literature on mobile technology as it relates to prevention and management of CVD. We also evaluate how apps can be used throughout all age groups with different CVD prevention needs.

Neubeck, L. *et al. Nat. Rev. Cardiol.* **12**, 350–360 (2015); published online 24 March 2015; doi:[10.1038/nrcardio.2015.34](https://doi.org/10.1038/nrcardio.2015.34)

# Incorporating Digital Technologies

Xu et al. *BMC Cardiovascular Disorders* (2019) 19:166  
<https://doi.org/10.1186/s12872-019-1149-5>


BMC Cardiovascular Disorders

RESEARCH ARTICLE

Open Access

## The effect of mobile applications for improving adherence in cardiac rehabilitation: a systematic review and meta-analysis



Linqi Xu<sup>1</sup>, Feng Li<sup>1</sup>, Changli Zhou<sup>1</sup>, Jinwei Li<sup>1</sup>, Chengcheng Hong<sup>2</sup> and Qian Tong<sup>3\*</sup> 

**Conclusion:** The use of mobile applications for improving the adherence of the CR might be effective. However, it appears to be in the initial stage of implementing mobile applications in CR and more research is essential to validate their effectiveness.

## Potential Disadvantages of Home-Based CR

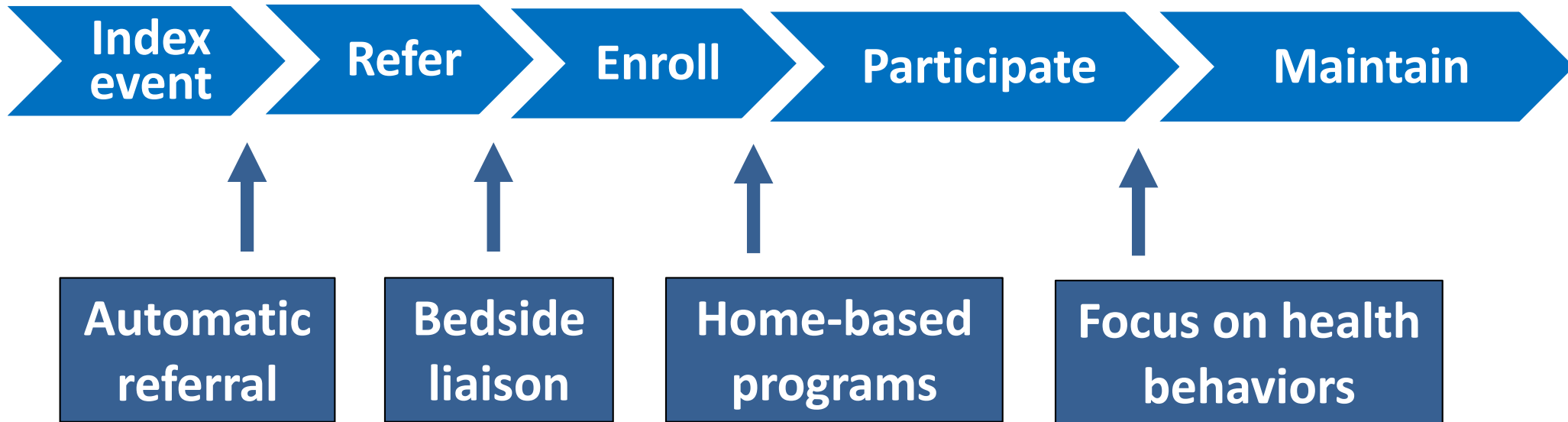
- Lack of reimbursement
- Less intensive exercise training
- Less social support
- Less patient accountability
- Lack of standardization among programs
- Less face-to-face monitoring and communication
- Safety concerns for higher-risk patients

## Potential Advantages of Home-Based CR

- Integration with regular home routine
- Reduced enrollment delays
- Expanded capacity/access
- Individually tailored
- Flexible, convenient scheduling
- Minimal travel/transportation barriers
- Patient privacy
- Potentially greater adherence and sustainability

- **Most importantly, home-based cardiac rehabilitation is better than nothing!**

# Quality Gaps = Opportunities for Improvement



# Cardiac Rehabilitation is Too Complicated

## 10 Key Components of CR

- Physical activity
- Medication adherence
- Smoking cessation
- Healthy eating
- Psychosocial support
- Blood pressure control
- Lipid management
- Diabetes management
- Weight management
- Outcome assessment



# Cardiac Rehabilitation is Too Complicated

## 10 Key Components of CR

- Physical activity
- Medication adherence
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- Healthy eating
- Psychosocial support
- ~~Blood pressure control~~
- ~~Lipid management~~
- ~~Diabetes management~~
- ~~Weight management~~
- ~~Outcome assessment~~

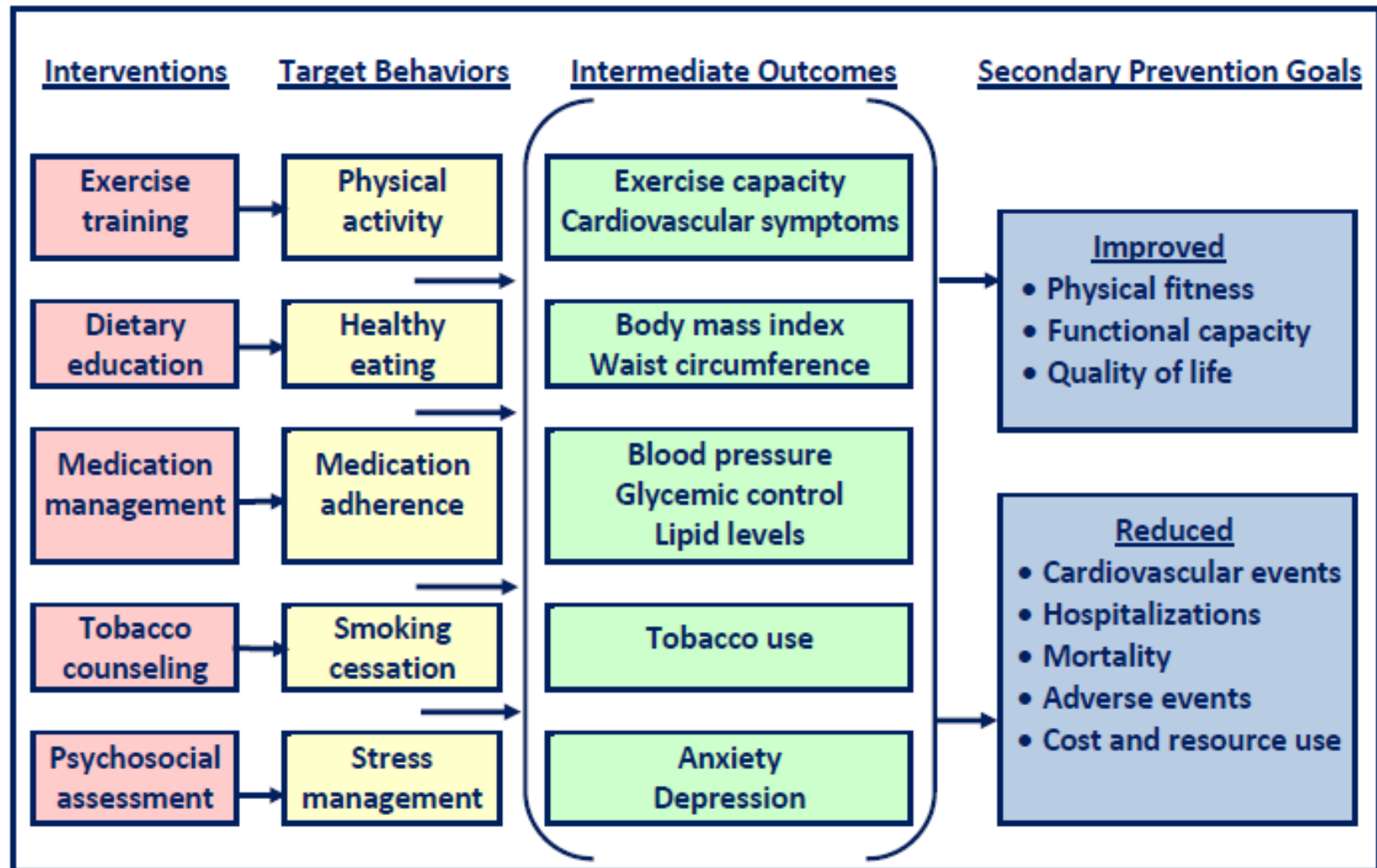


**Focus on the 5  
Behaviors that  
Patients Can Control**

**Focus on  
Modifiable  
Health  
Behaviors**



# Separate Structure, Process & Outcomes (Donabedian, 2005)



# CARDIAC REHABILITATION

## What is **CARDIAC REHABILITATION?**

### **1** Regular Exercise

From supervised activities, to a daily walk in the park, the idea is to get moving.



### **2** Adopt a Heart Healthy Diet

This includes meals that are low in salt and rich in whole grains, fruits, vegetables, low-fat meats and fish.



### **3** Reduce Stress

Learn to control your daily stress through relaxation techniques, recreation, music and other various methods.



### **5** Stop Smoking

Most cardiac rehab programs offer methods to help you kick this harmful habit.



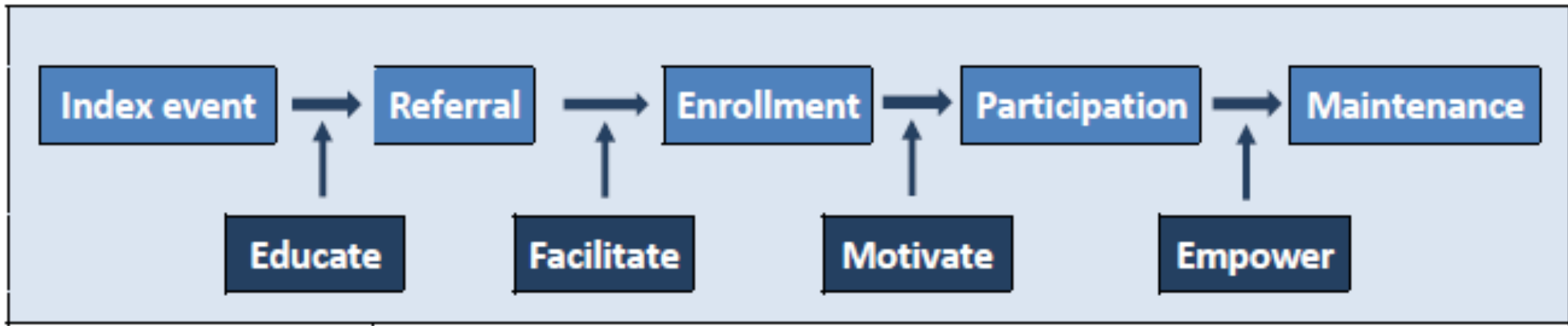
### **4** Medical Therapy

Follow your doctor's instructions carefully and take your medications as directed.



▶ For more information, visit [CardioSmart.org/CardiacRehab](https://www.CardioSmart.org/CardiacRehab)

## Track Metrics to Monitor Progress



Track:

- Number of days from index event to enrollment
- Number of patients referred (% of eligible)
- Number of patients enrolled (% of referred)
- Number of sessions completed

# Heart and Soul and Cardiac Rehabilitation



- Depression associated with adverse cardiovascular outcomes
- Key role of health behaviors (especially physical inactivity)
- Cardiac rehabilitation an underutilized opportunity to treat both
- Ways to improve engagement in cardiac rehabilitation
- **Potential benefits of COVID pandemic on cardiac rehab delivery**

## CARDIOLOGY NEWS

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# Pandemic Intensifies Push for Home-Based Cardiac Rehabilitation Options

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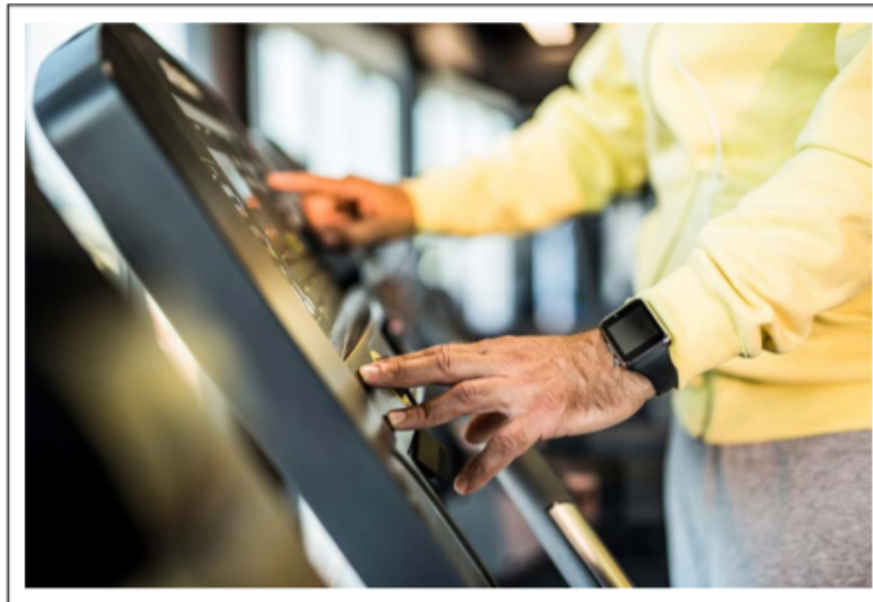
Bridget M. Kuehn

*Circulation. 2020;142:1781–1782.*

*DOI: 10.1161/CIRCULATIONAHA.120.051769*

**W**ith the coronavirus disease 2019 (COVID-19) pandemic shutting down 71% of in-center cardiac rehabilitation at least temporarily, according to a survey by the American Association of Cardiovascular and Pulmonary Rehabilitation, experiments with telehealth and mobile alternatives are receiving renewed attention. The statistics are particularly concerning because cardiac rehabilitation has been shown to reduce hospital readmission by 25% and death by 42%.

Cardiologist William Kraus, MD, distinguished university professor at Duke University Medical Center in Durham, North Carolina, and his colleagues ran a pilot study of a mobile technology-based cardiac rehabilitation program between March and



**Lockdowns associated with the ongoing pandemic have added a sense of urgency to develop mobile or telemedicine alternatives to in-center cardiac rehabilitation programs.**

# Cardiac Rehabilitation During COVID-19 Pandemic: Highlighting the Value of Home-Based Programs

Kariann R. Drwal, MS,<sup>1,2</sup> Daniel E. Forman, MD,<sup>3-5</sup>  
Bonnie J. Wakefield, PhD, RN,<sup>1,2,6</sup>  
and Ramzi N. El Accaoui, MD<sup>1,7</sup>

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## Introduction

**A**lthough most clinicians acknowledge the conceptual value of cardiac rehabilitation (CR), utilization of this class I treatment for cardiovascular disease (CVD) has remained low. Many reasons have been cited, particularly logistic impediments to accessing on-site-based programs (e.g., distance, transportation, scheduling, and availability). Although home-based CR (HBCR) has been increasingly advocated as a potential solution to the problem,<sup>1</sup> published data validating home-based options comparative effectiveness to center-based models with respect to patient outcomes (primarily function and quality-of-life measures) have utilized inconsistent protocols and most have been restricted to patient populations with relatively lower risk profiles.<sup>2-4</sup> Thus, many clinicians have remained skeptical about the utility of HBCR, especially for patients with higher CVD risks and/or clinical complexities. Lack of reim-



# Cardiac Rehabilitation Services during COVID-19 Pandemic

Bhargav Dave and Abhishek Jagtap

## ABSTRACT

Cardiac rehabilitation is a much appreciated but underutilized treatment strategy for cardiovascular disease. Traditional center-based cardiac rehabilitation program has been suspended due to the concrete measures adopted to flatten the COVID-19 pandemic curve. The current situation of emphasis the need of alternative approach for cardiac rehabilitation. This review shed light on consequences of COVID-19 disease on cardiac rehabilitation, the alternative approaches of cardiac rehabilitation, its potential advantages, and limitations as well as future directions.

**Keywords:** Coronavirus disease-2019, SARS-CoV-2, rehabilitation.

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# **The future is now: a call for action for cardiac telerehabilitation in the COVID-19 pandemic from the secondary prevention and rehabilitation section of the European Association of Preventive Cardiology**

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## Heart and Soul and Cardiac Rehabilitation



- Adverse cardiovascular outcomes associated with depression largely explained by poor health behaviors
- Cardiac rehab an opportunity to improve mental and physical health
- Automatic referral, bedside liaison, and home-based cardiac rehab can improve participation
- Focusing on the five modifiable health behaviors simplifies message
- “The future is now” – potential benefits of COVID pandemic