Published in final edited form as:

Circ Cardiovasc Qual Outcomes. 2016 January ; 9(1): 55–63. doi:10.1161/CIRCOUTCOMES.115.002184.

The Effects of Optimism and Gratitude on Physical Activity, Biomarkers, and Readmissions Following an Acute Coronary Syndrome: The Gratitude Research in Acute Coronary Events (GRACE) Study:

Huffman et al: Effects of Optimism and Gratitude After ACS

Jeff C. Huffman, MD^{1,2}, Eleanor E. Beale, BA², Christopher M. Celano, MD^{1,2}, Scott R. Beach, MD^{1,2}, Arianna M. Belcher, BS³, Shannon V. Moore, BA², Laura Suarez, MD^{1,2}, Shweta R. Motiwala, MD^{1,4}, Parul U. Gandhi, MD^{1,3}, Hanna Gaggin, MD^{1,3}, and James L. Januzzi, MD^{1,3}

¹Harvard Medical School, Boston, MA

²Department of Psychiatry, Massachusetts General Hospital, Boston, MA

³Department of Medicine, Division of Cardiology, Massachusetts General Hospital, Boston, MA

⁴Department of Medicine, Division of Cardiology, Beth Israel Deaconess Medical Center, Boston, MA

Abstract

Background—Positive psychological constructs, such as optimism, are associated with beneficial health outcomes. However, no study has separately examined the effects of multiple positive psychological constructs on behavioral, biological, and clinical outcomes after an acute coronary syndrome (ACS). Accordingly, we aimed to investigate associations of baseline optimism and gratitude with subsequent physical activity, prognostic biomarkers, and cardiac rehospitalizations in post-ACS patients.

Methods and Results—Participants were enrolled during admission for ACS and underwent assessments at baseline (2 weeks post-ACS) and follow-up (6 months later). Associations between baseline positive psychological constructs and subsequent physical activity/biomarkers were analyzed using multivariable linear regression. Associations between baseline positive constructs and 6-month rehospitalizations were assessed via multivariable Cox regression.

Overall, 164 participants enrolled and completed the baseline 2-week assessments. Baseline optimism was significantly associated with greater physical activity at 6 months ($n=153$; $\beta=102.5$; 95% confidence interval [13.6-191.5]; $p=.024$), controlling for baseline activity and sociodemographic, medical, and negative psychological covariates. Baseline optimism was also associated with lower rates of cardiac readmissions at 6 months ($N=164$), controlling for age, gender, and medical comorbidity (hazard ratio=.92; 95% confidence interval [.86-.98]; $p=.006$).

Correspondence to: Jeff C. Huffman, MD, Massachusetts General Hospital / Blake 11, 55 Fruit Street Boston, MA 02114, Phone: 617-724-2910, Fax: 617-724-9150, jhuffman@partners.org.

Disclosures: None.

There were no significant relationships between optimism and biomarkers. Gratitude was minimally associated with post-ACS outcomes.

Conclusions—Post-ACS optimism, but not gratitude, was prospectively and independently associated with superior physical activity and fewer cardiac readmissions. Whether interventions that target optimism can successfully increase optimism or improve cardiovascular outcomes in post-ACS patients is not yet known, but can be tested in future studies.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT01709669.

Keywords

exercise; angina; myocardial infarction; acute coronary syndrome; readmission; optimism; gratitude

Over 2.5 million persons worldwide are hospitalized each year for an acute coronary syndrome (ACS; myocardial infarction or unstable angina).¹ Among post-ACS patients, approximately 20% will be rehospitalized for ischemic heart disease or suffer mortality within the next year.² It is therefore critical to identify factors that may protect against adverse events and improve prognosis during the high-risk post-ACS period.

Positive psychological factors (e.g., positive affect, optimism) may have a beneficial impact on cardiac prognosis. Syntheses of the literature have found that positive psychological well-being is associated with superior cardiac health³ and reduced mortality⁴ in patients with medical illness, independent of traditional cardiac risk factors and negative psychological conditions (e.g., depression).

Among these positive psychological factors, optimism (a general expectation that the future will be favorable) may be most strongly associated with superior medical outcomes in those with and without known heart disease, with longitudinal studies⁵ and a comprehensive meta-analysis finding links between optimism and superior cardiac prognosis.⁶ In addition, gratitude (a disposition toward appreciating and being thankful for people, events, and experiences in one's life) is a common and often powerful experience following an ACS, with approximately one-half of patients reporting increased gratitude in the post-ACS period.⁷ The effects of gratitude on post-ACS recovery are worthy of investigation given its prevalence and the beneficial effects of other positive psychological constructs on cardiac health.

Prior studies suggest that psychological well-being may affect cardiac prognosis through superior adherence to key cardiac health behaviors, especially physical activity,⁸⁻¹⁰ that are associated with reduced rates of recurrent events and death after ACS.¹¹ In addition, some studies have shown positive psychological well-being to be associated with lower levels of circulating biomarkers associated with cardiac mortality,¹² such as inflammatory markers (e.g., interleukin-6 [IL-6]) and lipid levels.^{13, 14}

However, critical gaps in the literature exist. First, there has been minimal study of the prospective impact of positive psychological constructs in post-ACS patients⁸ despite the

ongoing need to identify factors that affect prognosis in this high-risk population. Second, despite the potential importance of gratitude on post-ACS recovery, there has been no prior study of the association of gratitude with clinical outcomes. Third, relatively few studies exploring positive psychological constructs and health outcomes have examined more than one positive state to assess whether one construct may be more or less prognostically important.^{15, 16} Finally, no prior investigation in this field has simultaneously examined the effects of positive psychological well-being on biological, behavioral, and clinical outcomes to most broadly understand the specific health effects of positive constructs.

Accordingly, in the Gratitude Research in Acute Coronary Events (GRACE) study, we examined the prospective effects of optimism and gratitude, measured 2 weeks post-ACS, on: (1) subsequent physical activity, (2) levels of inflammatory and other prognostic biomarkers, and (3) rates of cardiac readmission, over the next 6 months. We hypothesized that both optimism and gratitude would be associated with superior outcomes in all three domains, independent of multiple relevant covariates.

Methods

Overview

The GRACE study (clinicaltrials.gov identifier NCT01709669) was a prospective observational study that enrolled participants who were hospitalized for an ACS between September 2012 and January 2014. Study methods are described in additional detail elsewhere.¹⁷ In short, participants were enrolled in the hospital and completed study assessments 2 weeks post-ACS and 6 months later. The primary study outcome measure was physical activity in steps, measured via accelerometer, at 6 months. The original study enrollment goal was 150 participants. Approval from our healthcare system's Institutional Review Board was obtained prior to all study procedures, and full consent was obtained from all participants.

Study criteria and recruitment

Eligible patients were those admitted to one of three cardiac units at an urban academic medical center with a primary admission diagnosis of ACS, confirmed using established consensus guidelines and standardized criteria used in prior studies.^{18, 19}

Patients were excluded if they had: (1) a periprocedural ACS, (2) a condition likely to alter biomarkers of interest (e.g., renal failure, systemic lupus erythematosus), (3) a medical condition likely to be terminal within the timeframe of the study, (4) an unrelated condition limiting physical activity, (5) inability to communicate in English, or (6) cognitive disturbance that precluded participation or informed consent, as identified using a six-item cognitive screen designed to assess suitability for research participation.²⁰ Determination of exclusion criteria were made in conjunction with the primary medical team (e.g., regarding comorbid or terminal conditions). When ACS diagnosis or exclusionary conditions required further clarification, a senior study team cardiologist (HG or JJ) provided adjudication.

To recruit participants, patients admitted to the cardiac units for ACS were identified via patient census lists. Those who agreed to discuss an optional study and subsequently met the

above study criteria upon evaluation by study staff then underwent informed written informed consent if they wished to enroll.

Overview of assessment procedures

Following enrollment in the hospital, participants completed a detailed measure of pre-admission physical activity via the Physical Activity Recall (PAR) 7-day recall scale.²¹ The PAR has been widely used for research across multiple age groups and populations for 30 years.^{22, 23} It is easy for interviewers to administer with high reliability, and it detects change over time.²⁴ While accelerometers are the gold standard for measuring physical activity, the PAR correlates with accelerometry as well as or better than other self-report instruments.²⁵ Given that accelerometers could not be used at baseline due to the design of the study, we felt that the PAR would represent a feasible, reliable, and valid option that was not overly cumbersome for participants. Along with the PAR, staff obtained baseline sociodemographic characteristics and medical data via participant interview and electronic medical record review.

At the 2-week baseline in-person study visit, participants completed self-report measures, and blood was collected for baseline biomarker assessment. Participants wore accelerometers in the 2 week window prior to the final 6-month assessment to provide an objective measurement of physical activity. At the 6-month visit, biomarker collection and self-report measures were repeated, accelerometers were returned, and information about readmissions was collected (see Supplemental Figure 1 to view study assessments performed at each time point).

Study measures

Positive psychological variables—Optimism was measured using the six-item Life Orientation Test-Revised (LOT-R),²⁶ a well-established measure of dispositional optimism. Internal consistency of the LOT-R in this study was good (Cronbach's $\alpha=.85$). Gratitude was measured using the Gratitude Questionnaire-6 (GQ-6),²⁷ a brief, validated, six-item measure of dispositional gratitude, with good internal consistency in this cohort ($\alpha=.84$).

Negative psychological variables—Depression and anxiety were measured to control for these variables in our analyses. We assessed depression using the Patient Health Questionnaire-9 (PHQ-9),²⁸ a nine-item scale inquiring about the frequency of the nine symptoms of major depression in the prior two weeks; the PHQ-9 has good sensitivity and specificity for major depression in patients with heart disease.²⁹ For anxiety, we utilized the seven-item Hospital Anxiety and Depression Scale anxiety subscale (HADS-A).³⁰ This scale is designed for use with medically ill patients and has been used in studies of cardiac patients.³¹ Internal consistency of these measures was also high in this sample ($\alpha=.82$ and $\alpha=.85$, respectively).

Physical activity (Aim #1; primary study outcome)—Physical activity was chosen as the primary outcome measure because it is a key modifiable risk factor in ACS patients,^{11, 32} and prior studies have found that both dispositional optimism and interventions targeting gratitude have been associated with increased physical activity.^{9, 33}

Population studies find that objective measures must be used to accurately assess activity.³⁴ In this study, physical activity in steps per day was measured using the Fitlinxx Pebble uniaxial accelerometer (Fitlinxx, Shelton, CT). Similar to other published protocols for measuring physical activity,³⁵ we considered 6 valid days of wear (8 confirmed hours of wear time per day) to be sufficient. If participants failed to achieve adequate step data collection, they re-wore the devices.

We selected the Fitlinxx devices for several reasons. In this population of hospitalized patients, we highly prioritized simple, non-invasive measurement methods to encourage participation and full completion of the physical activity assessment protocol; the Pebble is a small (half-dollar coin-sized) device that fits non-invasively on belts or shoes. We also prioritized accuracy, and found on our own testing that step counts recorded with these devices matched manual step counts better than other noninvasive devices. Though the Fitlinxx devices are classified as accelerometers, they have been most often validated and used to count steps rather than examine activity intensity or caloric expenditure,³⁶ and we therefore decided upon mean steps/day as the primary activity outcome variable.

To control for baseline physical activity preceding the ACS, the 7-day PAR was used to recall activity in the 7 symptom-free days prior to admission. The PAR has good test-retest reliability and correlates with activity measured by diary and accelerometer in medically ill persons.³⁷ We chose to administer this measure in the hospital given the level of detail required for this assessment; waiting until the 2-week visit to obtain this information may have resulted in less detailed or less accurate recollection of baseline activity prior to hospitalization.

Biomarkers (Aim #2)—We collected prognostic biomarkers at 2 weeks and 6 months. We focused primarily on circulating markers related to systemic inflammation given that coronary heart disease is increasingly understood as a disorder of inflammation³⁸ and that there are established links between these markers and adverse prognosis in cardiac patients.¹²

We measured four commonly studied prognostic markers associated with inflammation: *high sensitivity C-reactive protein (hsCRP)*, *IL-6*, *tumor necrosis factor-alpha (TNF-α)*, and *soluble intracellular adhesion molecule-1 (sICAM-1)*; an endothelial adhesion molecule that mediates pathways responsible for vascular inflammation). We also measured *N-terminal pro-B-type natriuretic peptide (NT-proBNP)*, a marker associated with overall mortality risk after ACS.³⁹ Samples were analyzed in batch by immunoassay kits, as per published methods, via the MGH Research Core Laboratory (hsCRP, sICAM-1) and the Singulex Corporation (IL-6, TNF-α, NT-proBNP).

Rehospitalizations (Aim #3)—Our main readmissions outcome was non-elective cardiac readmissions. Data on readmissions was triangulated from participants, care providers, and health records to obtain the most complete information regarding these medical events. Participants were queried about all readmissions at the 6-month follow-up assessment, with data systematically gathered about timing of admission, symptoms, cause, and treatment. Study staff also contacted patients' primary medical and/or cardiology providers at the end

of the 6-month study period to inquire about readmissions and their cause, to assist in adjudication of admission diagnosis and to identify additional admissions not identified by participants.

Finally, participants' electronic medical records across the participating hospital's healthcare system (which includes ten acute care hospitals, several subacute settings, and numerous community health centers throughout the hospital's metropolitan area) were systematically reviewed over the 6-month follow-up timeframe. For admissions outside this system, additional records were obtained to identify principal diagnosis and other specific details, as required. All future admissions that had been planned at the time of discharge from the index admission (e.g., readmission for sequential cardiac stent placement in those with complex lesions) and any elective admissions were excluded from the analysis. Determination of cardiac (versus non-cardiac) cause for readmissions was made based on all available data including principal diagnosis; when unclear, this determination was adjudicated by study cardiologists.

We selected cardiac readmissions as the main outcome for this aim given that hospitalized patients may have a variable burden of other medical conditions for which they may be hospitalized and that cardiac readmissions would be most relevant to understanding the effects of optimism and gratitude on cardiac health. As an exploratory outcome, we also collected data on non-elective all-cause admissions.

Statistical analysis

Because the study examined the effects of 2-week psychological status on subsequent outcomes, participants must have completed 2-week assessments to be included in study analyses. Descriptive statistics (e.g., means, proportions, and standard deviations) were used to characterize the study population's baseline sociodemographic and medical characteristics, and their scores on baseline outcome measure assessments.

Aim #1 (Primary Aim): Association of baseline optimism and gratitude, measured 2 weeks post-ACS, with physical activity measured by accelerometer 6 months later—We examined associations of baseline LOT-R (optimism) and GQ-6 (gratitude) scores with mean number of daily steps 6 months later, via multivariable linear regression. To control for relevant covariates, we used a hierarchical series of models with increasing covariate adjustment. In the minimally-adjusted model (Model 1), we included the positive psychological variable (optimism or gratitude), age, and gender. In Model 2 (social and medical factors), we added a marker of social support (living alone), measures of ACS severity and history (peak troponin T and prior ACS), and a measure of overall medical comorbidity (the Charlson comorbidity index⁴⁰). Finally, in the fully adjusted model (Model 3), we added measures of depression and anxiety (PHQ-9 and HADS-A). For this outcome, in Models 2 and 3 we also controlled for baseline physical activity using the 7-day PAR. In all models, we used linear regression with bootstrap standard errors to account for any departures from normality of the residuals. For this primary analysis, we also completed sensitivity analyses to assess for significant differences

in the effects of optimism/gratitude on outcomes between men and women, and between White and non-White participants.

Aim #2: Association of baseline optimism/gratitude at 2 weeks with prognostic cardiac biomarkers at 6 months—We examined levels of each biomarker (hsCRP, IL-6, TNF- α , sICAM-1, NT-proBNP) separately 6 months post-baseline as the dependent variable. We performed multivariable analyses using linear regression, with hierarchical adjustment over the three successive models as above. Given departures from normality in the distribution of biomarker values, the values were log-transformed, and bootstrap standard errors were used to account for any residual non-normality. In secondary analyses, we completed identical analyses that also controlled for baseline levels of the biomarkers at 2 weeks within each model.

Aim #3: Association of baseline optimism/gratitude with rehospitalizations over the following 6 months—We performed time-to-event analyses to assess these associations. In preliminary analyses, we divided baseline LOT-R and GQ-6 scores at the median split and examined between-group differences in non-elective cardiac rehospitalizations using Kaplan-Meier curves and log-rank tests of significance. For our primary analyses, we utilized multivariable Cox regression to examine connections between continuous LOT-R and GQ-6 scores and rehospitalizations. We controlled for age and gender in the primary model; additional covariates were not included in the model because of the risk of overfitting based on the expected rate of rehospitalization (15%²). However, in an exploratory model, we additionally controlled for overall medical burden/comorbidity (Charlson Comorbidity Index) given the substantial effects of comorbid conditions on post-ACS readmission rates.⁴¹ We then repeated all analyses for all-cause (non-elective) rehospitalizations as an outcome variable.

All analyses were performed using Stata statistical software (PC version 11.2, StataCorp, College Station, TX). For our initial enrollment goal of 150 participants, assuming follow-up data from 85% of subjects (consistent with our similar prior studies^{31, 42}), and an estimated moderate effect size ($\rho=.3$) of positive psychological constructs on activity (univariate), the study was powered at 94% to detect a significant association between both positive psychological constructs and physical activity in steps. All tests were two-tailed. Statistical significance was set at $p<.05$ for all aims, though a very conservative correction for multiple comparisons in the Aim #2 biomarker analyses using a Bonferroni correction would have set the p value for significance at $p<.01$.

Results

Figure 1 presents the CONSORT diagram for GRACE. Among 212 patients who were enrolled in-hospital, 164 successfully completed the 2-week baseline visit. Rehospitalization data at 6 months was available from all 164 participants; adequate physical activity data was collected from 153 participants (93%) at 6 months, and biomarker data was collected from 152 (92%).

Baseline sociodemographic characteristics, medical variables, psychiatric status, and baseline study outcome variables are listed in Table 1. Overall, the mean age of subjects was 61.5 (standard deviation [SD] 10.5) years, 84% were men, and 84% were White. This was the first ACS for 58% of participants. These baseline variables are also displayed, split by median baseline gratitude (GQ-6) and optimism (LOT-R) scores, in Supplemental Table 1.

With respect to baseline psychological variables (2-week visit), participants had a mean LOT-R score of 17.7 (SD 5.6), higher than general population norms for this age group (14.8 [SD 3.4]),⁴³ and a mean GQ-6 score of 36.5 (SD 5.8), consistent with published norms (36.9 [SD 4.9]).²⁷ Depression (PHQ-9: mean score 4.4 [SD 4.5]) and anxiety (HADS-A: mean score 4.3 [SD 4.0]) scores were below established cutoffs for clinically significant depression (PHQ-9 ≥ 10) or anxiety (HADS-A ≥ 8), and were slightly lower than mean values in other cardiac populations (PHQ-9=4.8; HADS-A=6.8).^{44, 45}

Aim #1: Physical activity (Table 2)

Participants took a mean 5147 (SD 2836) steps per day. Baseline optimism (LOT-R) was associated with an increased number of steps when controlling for age and gender (Model 1; $\beta=94.4$, 95% confidence interval [CI; 26.5, 162.2], $p=.006$), when additionally controlling for social and medical variables including pre-ACS physical activity (Model 2; $\beta=99.3$, 95% CI [32.6, 166.0], $p=.004$), and in the fully adjusted model that included depression and anxiety (Model 3; $\beta=102.5$, 95% CI [13.6, 191.5], $p=.024$). In contrast, baseline gratitude (GQ-6) was not associated with physical activity ($p>.10$) in any of the models. There were no significant differences in the associations between the positive psychological constructs and steps between men and women, or between White and non-White participants ($p>.05$ for all analyses).

Aim #2: Biomarkers (Supplemental Table 2)

Adjusting for age and gender, baseline optimism was associated with hsCRP 6 months post-baseline ($\beta=-.04$, 95% CI [-.08, -.007], $p=.020$), though the association became marginal when controlling for social and medical variables ($\beta=-.03$, 95% CI [-.07, .003], $p=.075$) and when depression and anxiety were added to the model ($\beta=-.04$, 95% CI [-.08, .003], $p=.071$).

Regarding sICAM-1, adjusting for age and gender, baseline optimism was associated with sICAM-1 ($\beta=-.012$, 95% CI [-.021, -.002], $p=.019$), though the association became marginal when controlling for social and medical variables ($\beta=-.009$, 95% CI [-.019, .0006], $p=.067$) and was non-significant ($p>.10$) when depression and anxiety were added to the model.

Baseline optimism was associated with TNF- α , controlling for age and gender ($\beta=-.012$, 95% CI [-.022, -.002], $p=.019$), and when additionally controlling for social and medical variables ($\beta=-.012$, 95% CI [-.021, -.003], $p=.009$); this association became non-significant when depression and anxiety were added. Baseline gratitude was associated with TNF- α in all three models (fully adjusted model: $\beta=-.009$, 95% CI [-.018, -.0004], $p=.039$). There were no associations between positive psychological constructs and IL-6 or NT-proBNP, and no significant associations when 2-week biomarker levels were added to the model (Supplemental Table 3).

Aim #3: Rehospitalizations (Table 2)

Over the 6-month follow-up period, 35 (21.3%) patients had a readmission for any cause, and 28 (17.1%) had a non-elective cardiac readmission. On preliminary time-to-event analysis using a median split (LOT-R 19 vs. 20), baseline optimism was marginally associated with non-elective cardiac readmissions over the following 6 months (Kaplan-Meier Curve, Figure 2; log-rank test, $\chi^2=3.31$; $p=.069$). On main analysis via Cox regression, baseline optimism was associated with fewer non-elective cardiac readmissions (Hazard Ratio [HR]=.92, 95% CI [.86, .97], $p=.005$), controlling for age and gender. On exploratory analysis including medical comorbidity (Charlson index) in the model, optimism remained associated with non-elective cardiac readmissions (HR=.92, 95% CI [.86, .98], $p=.006$).

Regarding all-cause readmissions, baseline optimism was not associated with non-elective readmissions over 6 months on preliminary analysis (Supplemental Figure 2; log-rank test, $\chi^2=1.22$; $p=.27$). However, on Cox regression, baseline optimism was associated with fewer non-elective readmissions controlling for age and gender (HR=.94, 95% CI [.89, .997], $p=.040$), and when including the Charlson index (HR=.94, 95% CI [.89, .998], $p=.043$).

Gratitude was not associated with rehospitalizations using median split (GQ-6 37 vs. 38; Supplemental Figures 3 and 4) or continuous GQ-6 scores.

Discussion

This was the first study to concurrently examine the effects of multiple positive psychological constructs on outcomes in ACS patients, a population at substantial risk for poor health, rehospitalizations, and mortality. It was also the first to examine the prospective effects of these positive constructs on health behaviors, prognostic biomarkers, and clinical outcomes within the same study to explore possible mechanisms by which these constructs may confer benefit.

We found that optimism, measured 2 weeks after ACS, was associated with greater physical activity in mean steps/day at 6 months, controlling for pre-ACS physical activity and numerous baseline demographic and medical factors. The relationship between optimism and physical activity also held when controlling for depression and anxiety, suggesting a unique effect of *positive* psychological well-being on post-ACS physical activity. Confidence intervals for physical activity were wide, given the substantial variability in number of mean steps taken by participants.

These results are consistent with prior studies finding optimism to be associated with increased levels of activity, though many of these prior studies were cross-sectional in nature or utilized non-clinical populations,^{9, 10, 32} and none had objectively measured activity. To our knowledge, only one prior study assessed optimism and physical activity following an ACS.⁸ In a well-designed observational study by Ronaldson and colleagues,⁸ post-ACS optimism measured by the LOT-R was associated with several cardiac health behaviors but not with post-ACS physical activity at 12 months. However, physical activity in that study was measured solely by self-report. Our finding that higher optimism predicts greater increases in objectively measured activity has substantial clinical relevance given

that increasing physical activity after an ACS is associated with fewer recurrent events and lower rates of death.¹¹

In contrast, optimism was not strongly associated with inflammatory biomarkers or NT-proBNP at 6 months. In prior work, relationships between positive psychological variables and biomarkers have generally been less consistent than connections of these variables to health behaviors,³ and this was true in our study population. This suggests that benefits from positive psychological states may be more related to behavior than to a direct decrease in systemic inflammation or other circulating markers, at least in the early post-ACS period. Whether a longer follow-up period would have revealed more robust associations between optimism and biomarkers remains unclear.

Finally, and of note, optimism at 2 weeks was associated with reduced rates of non-elective cardiac readmissions at 6 months, independent of age, gender, and (on exploratory analysis) medical comorbidity, with each point on the LOT-R associated with an 8% reduction in risk of rehospitalization. These findings also held for all-cause readmissions, though this relationship was largely driven by rates of cardiac readmission. Given the high rates of cardiac readmissions in post-ACS patients,⁴⁶ this finding may have substantial clinical relevance. Prevention of early readmissions is a major initiative across Western healthcare systems to improve patient outcomes and reduce costs,⁴⁷ and optimism may be one patient-level factor associated with reduced readmissions.

In contrast to the effects of optimism, baseline gratitude was not associated with behavioral, biological, or clinical outcomes in this cohort, aside from an association with 6 month TNF- α . This finding suggests that not all positive psychological constructs necessarily have the same effect on medical and behavioral outcomes and that it is important to examine specific psychological constructs within the field of psychological well-being. In ACS patients, gratitude, with an inward positive focus on past and current events, may have had a lesser effect on future orientation and subsequent behavior compared to optimism, which is by its nature future-focused. Our findings are consistent with qualitative research in ACS patients finding that, while optimism and gratitude are both common after ACS, only optimism is associated with initiation of physical activity and other health behaviors.⁴⁸

Why might optimism, but not gratitude, affect health outcomes? First, optimism focuses on future expectations. Given that that our outcomes were focused on events that happened post-assessment (e.g., whether participants became more active), believing that one's future (and future health) were likely to improve may have played a substantial role in their motivation and confidence to make change. In contrast, gratitude is largely a current- or past-focused construct, in which people experience well-being by taking stock of their immediate and prior experiences. Second, optimism in many cases can be a more action-based cognition—a sense that one can do something to reach a goal—which may promote beneficial changes in health behavior. Thoughts or expressions of gratitude may be less directly linked to making behavioral changes.

This observational study had several important limitations. It occurred at a single academic site and enrolled a preponderance of White men, potentially limiting generalizability; the

lack of significant differences in outcomes by sex and race may have been due to limited power given the relatively small number of women and non-White participants. To address this issue, we considered limiting recruitment of White men mid-study. However, after review, we concluded that having a greater number of total participants—thus increasing the power to detect significant relationships between positive psychological constructs and outcomes—was the greatest priority for this initial trial. Approximately 20% of initially enrolling participants did not provide baseline data, typically because of intervening medical issues prior to the 2-week baseline visit, though over 90% of those who provided baseline data completed all components of the 6-month assessments. We measured steps/day rather than activity intensity, and though step counts correlate well with overall observed activity,⁴⁹ more comprehensive activity assessment devices are available. We also did not obtain objective follow-up data about other health behaviors. Finally, the 6 month period for assessing readmissions, while representing a critical high-risk period, was relatively short and limited analytic power.

Despite these limitations, this study suggests a distinct contribution of optimism to increased physical activity and readmission reduction during the critical post-ACS period. The effects of optimism on physical activity were above and beyond the adverse effects of depression and anxiety, and were in contrast to gratitude, which was not linked to outcomes. These findings suggest that optimism, if measured shortly after an ACS, could be used as a novel predictor of reduced physical activity or readmissions. Our findings likely also apply to other conditions, such as hypertension or type 2 diabetes, for which increasing physical activity and other health behaviors may be critical in slowing disease progression or reducing mortality. These findings are also relevant to the prevention of chronic illnesses, given the benefits of physical activity in preventing a wide range of conditions. Furthermore, key questions remain: is it possible to promote optimism in patients with cardiovascular illness, and will such interventions result in improvement in clinical outcomes? A pair of randomized trials in hypertension and heart disease found a positive affect-based program to be associated with superior improvements in physical activity and other health behaviors.^{39, 50} Future studies are required to determine whether similar programs are effective in ACS patients and whether they can modify prognosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Ms. Kirsti Campbell for her assistance in revising and editing this manuscript in preparation for submission.

Sources of Funding: This research project was supported by the Expanding the Science and Practice of Gratitude Project run by UC Berkeley's Greater Good Science Center in partnership with UC Davis with funding from the John Templeton Foundation (grant 15627) to JH. Time for analysis and manuscript preparation was also funded by National Institutes of Health under grant R01HL113272 to JH. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The Harvard Catalyst Program and the Singulex Corporation provided support for analysis of selected biomarkers.

References

1. Grech ED, Ramsdale DR. Acute coronary syndrome: unstable angina and non-ST segment elevation myocardial infarction. *BMJ*. 2003; 326:1259–1261. [PubMed: 12791748]
2. Yeo KK, Fam JM, Lim ST, Lau YH, Sim LL, Chua T, Koh TH. Comparison of clinical characteristics, 1-year readmission rates, cost and mortality amongst patients undergoing percutaneous coronary intervention for stable angina, acute coronary syndromes and ST-elevation myocardial infarction. *EuroIntervention*. 2012; 8:295. [PubMed: 22829503]
3. DuBois CM, Lopez OV, Beale EE, Healy BC, Boehm JK, Huffman JC. Relationships between positive psychological constructs and health outcomes in patients with cardiovascular disease: a systematic review. *Int J Cardiol*. 2015; 195:265–280. [PubMed: 26048390]
4. Chida Y, Steptoe A. Positive psychological well-being and mortality: a quantitative review of prospective observational studies. *Psychosom Med*. 2008; 70:741–756. [PubMed: 18725425]
5. Tindle HA, Chang YF, Kuller LH, Manson JE, Robinson JG, Rosal MC, Siegle GJ, Matthews KA. Optimism, cynical hostility, and incident coronary heart disease and mortality in the Women's Health Initiative. *Circulation*. 2009; 120:656–662. [PubMed: 19667234]
6. Rasmussen HN, Scheier MF, Greenhouse JB. Optimism and physical health: a meta-analytic review. *Ann Behav Med*. 2009; 37:239–256. [PubMed: 19711142]
7. Laerum E, Johnsen N, Smith P, Larsen S. Myocardial infarction may induce positive changes in life-style and in the quality of life. *Scand J Prim Health Care*. 1988; 6:67–71. [PubMed: 3387709]
8. Ronaldson A, Molloy GJ, Wikman A, Poole L, Kaski JC, Steptoe A. Optimism and recovery after acute coronary syndrome: a clinical cohort study. *Psychosom Med*. 2015; 77:311–318. [PubMed: 25738438]
9. Giltay EJ, Geleijnse JM, Zitman FG, Buijsse B, Kromhout D. Lifestyle and dietary correlates of dispositional optimism in men: The Zutphen Elderly Study. *J Psychosom Res*. 2007; 63:483–490. [PubMed: 17980220]
10. Steptoe A, Wright C, Kunz-Ebrecht SR, Iliffe S. Dispositional optimism and health behaviour in community-dwelling older people: associations with healthy ageing. *Br J Health Psychol*. 2006; 11:71–84. [PubMed: 16480556]
11. Steffen-Batey L, Nichaman MZ, Goff DC Jr, Frankowski RF, Hanis CL, Ramsey DJ, Labarthe DR. Change in level of physical activity and risk of all-cause mortality or reinfarction: The Corpus Christi Heart Project. *Circulation*. 2000; 102:2204–2209. [PubMed: 11056093]
12. Kavsak PA, Ko DT, Newman AM, Palomaki GE, Lustig V, MacRae AR, Jaffe AS. Risk stratification for heart failure and death in an acute coronary syndrome population using inflammatory cytokines and N-terminal pro-brain natriuretic peptide. *Clin Chem*. 2007; 53:2112–2118. [PubMed: 17932131]
13. Brouwers C, Mommersteeg P, Nyklicek I, Pelle A, Westerhuis B, Szabo B, Denollet J. Positive affect dimensions and their association with inflammatory biomarkers in patients with chronic heart failure. *Biol Psychol*. 2013; 92:220–226. [PubMed: 23085133]
14. Ryff CD, Keyes CL. The structure of psychological well-being revisited. *J Pers Soc Psychol*. 1995; 69:719–727. [PubMed: 7473027]
15. Grunberg GE, Crater SW, Green CL, Seskevich J, Lane JD, Koenig HG, Bashore TM, Morris KG, Mark DB, Krucoff MW. Correlations between preprocedure mood and clinical outcome in patients undergoing coronary angioplasty. *Cardiol Rev*. 2003; 11:309–317. [PubMed: 14580299]
16. Jenkins CD, Stanton BA, Jono RT. Quantifying and predicting recovery after heart surgery. *Psychosom Med*. 1994; 56:203–212. [PubMed: 8084965]
17. Huffman JC, Beale EE, Beach SR, Celano CM, Belcher AM, Moore SV, Suarez L, Gandhi PU, Motiwala SR, Gaggin H, Januzzi JL. Design and baseline data from the Gratitude Research in Acute Coronary Events (GRACE) study. *Contemp Clin Trials*. 2015; 44:11–19. [PubMed: 26166171]
18. Ibrahim AW, Riddell TC, Devireddy CM. Acute myocardial infarction. *Crit Care Clin*. 2014; 30:341–364. [PubMed: 24996601]
19. Weisz G, Moses JW, Teirstein PS, Holmes DR Jr, Raizner AE, Satler LF, Mishkel G, Wilensky RL, Wang P, Kuntz RE, Popma JJ, Leon MB. Safety of sirolimus-eluting stenting and its effect on

- restenosis in patients with unstable angina pectoris (a SIRIUS substudy). *Am J Cardiol.* 2007; 99:1044–1050. [PubMed: 17437725]
20. Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med Care.* 2002; 40:771–781. [PubMed: 12218768]
 21. Sallis JF, Haskell WL, Wood PD, Fortmann SP, Rogers T, Blair SN, Paffenbarger RS Jr. Physical activity assessment methodology in the Five-City Project. *Am J Epidemiol.* 1985; 121:91–106. [PubMed: 3964995]
 22. Garfield BE, Canavan JL, Smith CJ, Ingram KA, Fowler RP, Clark AL, Polkey MI, Man WD. Stanford Seven-Day Physical Activity Recall questionnaire in COPD. *Eur Respir J.* 2012; 40:356–362. [PubMed: 22183486]
 23. Sallis JF, Calfas KJ, Nichols JF, Sarkin JA, Johnson MF, Caparosa S, Thompson S, Alcaraz JE. Evaluation of a university course to promote physical activity: project GRAD. *Res Q Exerc Sport.* 1999; 70:1–10. [PubMed: 10100330]
 24. Blair SN, Haskell WL, Ho P, Paffenbarger RS Jr, Vranizan KM, Farquhar JW, Wood PD. Assessment of habitual physical activity by a seven-day recall in a community survey and controlled experiments. *Am J Epidemiol.* 1985; 122:794–804. [PubMed: 3876763]
 25. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. *Res Q Exerc Sport.* 2000; 71:S1–14. [PubMed: 10925819]
 26. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. *J Pers Soc Psychol.* 1994; 67:1063–1078. [PubMed: 7815302]
 27. McCullough ME, Emmons RA, Tsang JA. The grateful disposition: a conceptual and empirical topography. *J Pers Soc Psychol.* 2002; 82:112–127. [PubMed: 11811629]
 28. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001; 16:606–613. [PubMed: 11556941]
 29. Lichtman JH, Bigger JT, Blumenthal JA, Frasure-Smith N, Kaufmann PG, Lesperance F, Mark DB, Sheps DS, Taylor CB, Froelicher ES. Depression and coronary heart disease. Recommendations for screening, referral, and treatment. *Circulation.* 2008; 118:1768–1775. [PubMed: 18824640]
 30. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res.* 2002; 52:69–77. [PubMed: 11832252]
 31. Huffman JC, Mastromauro CA, Beach SR, Celano CM, DuBois CM, Healy BC, Suarez L, Rollman BL, Januzzi JL. Collaborative care for depression and anxiety disorders in patients with recent cardiac events: the Management of Sadness and Anxiety in Cardiology (MOSAIC) randomized clinical trial. *JAMA Intern Med.* 2014; 174:927–935. [PubMed: 24733277]
 32. Browning C, Sims J, Kendig H, Teshuva K. Predictors of physical activity behavior in older community-dwelling adults. *J Allied Health.* 2009; 38:8–17. [PubMed: 19361018]
 33. Emmons RA, McCullough ME. Counting blessings versus burdens: an experimental investigation of gratitude and subjective well-being in daily life. *J Pers Soc Psychol.* 2003; 84:377–389. [PubMed: 12585811]
 34. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc.* 2008; 40:181–188. [PubMed: 18091006]
 35. Buman MP, Hekler EB, Haskell WL, Pruitt L, Conway TL, Cain KL, Sallis JF, Saelens BE, Frank LD, King AC. Objective light-intensity physical activity associations with rated health in older adults. *Am J Epidemiol.* 2010; 172:1155–1165. [PubMed: 20843864]
 36. Watson A, Bickmore T, Cange A, Kulshreshtha A, Kvedar J. An internet-based virtual coach to promote physical activity adherence in overweight adults: randomized controlled trial. *J Med Internet Res.* 2012; 14:e1. [PubMed: 22281837]
 37. McDermott MM, Liu K, O'Brien E, Guralnik JM, Criqui MH, Martin GJ, Greenland P. Measuring physical activity in peripheral arterial disease: a comparison of two physical activity questionnaires with an accelerometer. *Angiology.* 2000; 51:91–100. [PubMed: 10701716]

38. Linden F, Domschke G, Erbel C, Akhavanpoor M, Katus HA, Gleissner CA. Inflammatory therapeutic targets in coronary atherosclerosis-from molecular biology to clinical application. *Front Physiol.* 2014; 5:455. [PubMed: 25484870]
39. Peterson JC, Charlson ME, Hoffman Z, Wells MT, Wong SC, Hollenberg JP, Jobe JB, Boschert KA, Isen AM, Allegante JP. A randomized controlled trial of positive-affect induction to promote physical activity after percutaneous coronary intervention. *Arch Intern Med.* 2012; 172:329–336. [PubMed: 22269589]
40. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987; 40:373–383. [PubMed: 3558716]
41. Southern DA, Ngo J, Martin BJ, Galbraith PD, Knudtson ML, Ghali WA, James MT, Wilton SB. Characterizing types of readmission after acute coronary syndrome hospitalization: implications for quality reporting. *J Am Heart Assoc.* 2014; 3:e001046. [PubMed: 25237046]
42. Huffman JC, Mastromauro CA, Sowden G, Fricchione GL, Healy BC, Januzzi JL. Impact of a depression care management program for hospitalized cardiac patients. *Circ Cardiovasc Qual Outcomes.* 2011; 4:198–205. [PubMed: 21386067]
43. Glaesmer H, Rief W, Martin A, Mewes R, Brahler E, Zenger M, Hinz A. Psychometric properties and population-based norms of the Life Orientation Test Revised (LOT-R). *Br J Health Psychol.* 2012; 17:432–445. [PubMed: 22106985]
44. Stafford L, Berk M, Jackson HJ. Validity of the Hospital Anxiety and Depression Scale and Patient Health Questionnaire-9 to screen for depression in patients with coronary artery disease. *Gen Hosp Psychiatry.* 2007; 29:417–424. [PubMed: 17888808]
45. Doyle F, Conroy R, McGee H. Differential predictive value of depressive versus anxiety symptoms in the prediction of 8-year mortality after acute coronary syndrome. *Psychosom Med.* 2012; 74:711–716. [PubMed: 22923700]
46. Menzin J, Wygant G, Hauch O, Jackel J, Friedman M. One-year costs of ischemic heart disease among patients with acute coronary syndromes: findings from a multi-employer claims database. *Curr Med Res Opin.* 2008; 24:461–468. [PubMed: 18194592]
47. Joynt KE, Jha AK. Thirty-day readmissions--truth and consequences. *N Engl J Med.* 2012; 366:1366–1369. [PubMed: 22455752]
48. Huffman JC, DuBois CM, Mastromauro CA, Moore SV, Suarez L, Park ER. Positive psychological states and health behaviors in acute coronary syndrome patients: A qualitative study. *J Health Psychol.* 2014 Epub ahead of print.
49. Tudor-Locke C, Williams JE, Reis JP, Pluto D. Utility of pedometers for assessing physical activity: convergent validity. *Sports Med.* 2002; 32:795–808. [PubMed: 12238942]
50. Ogedegbe GO, Boutin-Foster C, Wells MT, Allegante JP, Isen AM, Jobe JB, Charlson ME. A randomized controlled trial of positive-affect intervention and medication adherence in hypertensive African Americans. *Arch Intern Med.* 2012; 172:322–326. [PubMed: 22269592]

What is Known

- Negative psychological constructs, such as depression and anxiety, are independently associated with worse prognosis following an acute coronary syndrome (ACS).
- However, little is known about the prospective relationship between positive psychological constructs (such as optimism and gratitude) and cardiac health following an ACS.

What the Study Adds

- Optimism, measured 2 weeks following an ACS, was prospectively and independently associated with greater physical activity and reduced rates of cardiac readmissions, but not prognostic biomarkers, over the following 6 months.
- In contrast, gratitude was not associated with physical activity, biomarkers, or readmissions over the same time period.
- Optimism may serve as a novel predictor of subsequent physical activity and fewer readmissions when measured shortly following an ACS.

Figure 1. Study recruitment and enrollment

Figure 2. Time to non-elective cardiac readmission split by baseline optimism scores (LOT-R 19 vs. 20)

Table 1
Baseline sociodemographic and clinical characteristics (N=164) in the GRACE study

Characteristics	N (%) [*]
Demographics and psychosocial characteristics	
Age (mean [SD])	61.5 (10.6)
Male sex	137 (84)
White	137 (84)
Married	113 (69)
Living alone	38 (23)
Medical history	
Body mass index (mean [SD])	28.9 (5.2)
Hypertension	103 (63)
Diabetes mellitus	34 (21)
Hyperlipidemia	132 (81)
Current smoking	21 (13)
Prior acute coronary syndrome	69 (42)
Admission diagnosis of myocardial infarction	88 (54)
Length of stay (days; mean [SD])	3.0 (2.0)
Troponin T	1.5 (3.5)
Charlson Index (age adjusted)	3.3 (1.6)
Medications at discharge	
Aspirin	159 (97)
Beta blocker	144 (88)
Angiotensin converting enzyme inhibitor/Angiotensin receptor blocker	90 (55)
Antiplatelet agents	127 (77)
Statin	153 (93)
Antidepressant	27 (17)
Anxiolytic	16 (10)
Self-report measures at baseline 2-week visit (mean [SD])	
Life Orientation Test-Revised (optimism; <i>range: 0-24</i>)	17.7 (5.6)
Gratitude Questionnaire-6 (gratitude; <i>range: 6 - 42</i>)	36.5 (5.8)
Patient Health Questionnaire-9 (depression; <i>range: 0-27</i>)	4.3 (4.4)
Hospital Anxiety and Depression Scale-Anxiety subscale (anxiety; <i>range: 0-21</i>)	4.3 (4.0)
Metabolic equivalents (Physical Activity Recall)	37.0 (8.5)
Biomarker levels at baseline 2-week visit (mean [SD])	
C-reactive protein	5.1 (9.3)
Interleukin-6	3.7 (4.1)
Soluble intercellular adhesion molecule-1	0.5 (0.2)
N-terminal pro-B-type natriuretic peptide	152 (192)

* All figures are N (%) unless otherwise specified.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Associations between baseline optimism/gratitude and 6-month physical activity and rehospitalizations, showing measures of effect

Table 2

Outcome	Model	Two week predictor variables			
		Optimism (LOT-R)		Gratitude (GQ-6)	
Physical Activity (Primary Study Outcome) <i>Mean steps/day</i>	1	β	CI	β	CI
		94.4 [*]	26.5, 162.2	43.9	-17.5, 105.2
	2	99.3 [*]	32.6, 166.0	55.4	-16.6, 127.4
	3	102.5 [†]	13.6, 191.5	34.8	-55.0, 124.5
Cardiac Readmissions		HR	CI	HR	CI
	1	0.92 [*]	0.86, 0.97	0.96	0.91, 1.02
	Exploratory	0.92 [*]	0.86, 0.98	0.96	0.91, 1.01
All-cause Readmissions	1	0.94 [†]	0.89, 1.0	0.97	0.92, 1.02
	Exploratory	0.94 [†]	0.89, 1.0	0.97	0.92, 1.02

Legend. β =regression coefficient; GQ-6=Gratitude Questionnaire-6; HR=Hazard Ratio; LOT-R=Life Orientation Test-Revised.

Model 1: controlling for age and gender

Model 2: controlling for Model 1 covariates plus living alone, prior acute coronary syndrome, peak troponin T, Charlson comorbidity index

Model 3: controlling for Model 2 covariates plus depression and anxiety

Exploratory Model (Readmissions): controlling for age, gender, and Charlson Comorbidity Index

^{*} p<.01,

[†] p<.05