Reduced positive affect (anhedonia) predicts major clinical events following implantation of coronary-artery stents

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Reduced positive affect (anhedonia) predicts major clinical events following implantation of coronary-artery stents

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Abstract. Denollet J, Pedersen SS, Daemen J, de Jaegere P, Serruys PW, van Domburg RT (Tilburg University, Tilburg; and Erasmus Medical Center, Rotterdam; The Netherlands). Reduced positive affect (anhedonia) predicts major clinical events following implantation of coronary-artery stents. *J Intern Med* 2008; **263**: 203–211.

Objective. Emotional distress has been related to clinical events in patients with coronary artery disease, but the influence of positive affect (i.e. mood states such as activity, joy and cheerfulness) has received little attention. Therefore, we wanted to investigate the role of positive affect on clinical outcome after percutaneous coronary intervention (PCI) with stent implantation in these patients.

Design. Prospective follow-up study. At baseline, patients from the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry completed measures of positive affect, depression and anxiety post-PCI. Patients with reduced positive affect scored 1 SD below the mean score.

Setting. University Hospital; Thoraxcenter of the Department of Cardiology.

Subjects. 874 patients (72% men; 62.2 ± 10.9 years) from the RESEARCH registry.

Main outcome measure. Death or myocardial infarction (MI) 2 years post-PCI.

Results. At follow-up, there were 52 clinical events (deaths $n = 27$, MIs $n = 25$). Reduced positive affect and depression/anxiety were associated with poor prognosis, but reduced positive affect was the only independent predictor of events. The incidence of death/MI in adequate versus reduced positive affect patients was 4% (29/663) vs. 11% (23/211); HR = 2.55 (95% CI 1.46–4.34, $P = 0.001$), adjusting for clinical variables. Reduced positive affect and diabetes were independent prognostic factors, and patients with one (HR = 2.84, 95% CI 1.58–5.10) or both (HR = 5.61, 95% CI 2.25–13.99) of these factors had a higher risk when compared with nondiabetic patients with adequate positive affect, $P \leq 0.003$.

Conclusions. Reduced positive affect independently predicted death/MI following stent implantation, and improved risk stratification above and beyond diabetes.

Keywords: coronary artery disease, diabetes, depression, positive affect, anhedonia.

Introduction

Symptoms of psychosocial distress have been associated with an increased risk of cardiac events [1–4]. However, little is known about the impact of positive affect. Positive affect refers to mood states such as joy, activity and cheerfulness [5]. Positive affect is not merely the opposite of negative affect [6], as

people can experience positive and negative emotions at the same time [7]. Epidemiological research in middle-aged adults [8] and patients with coronary artery disease (CAD) [9] has confirmed that these emotions are relatively independent mood dimensions.

Positive affect may enhance immune function [10] and one's ability to achieve successful outcomes in life [11], and dampen physiologic reactivity to stress [12]. Reduced positive affect has also been associated with an increased risk of mortality [13] and stroke [14] in community-based studies of older adults. By contrast, there is a paucity of research on the role of positive affect in surviving serious illness [5]. Positive affect may benefit survival in AIDS [15] and surgery [16] patients, but more research is needed on the effect of adequate versus reduced positive affect in cardiac patients. An advantage of studying positive affect is that CAD patients are not likely to describe themselves in terms of negative emotions alone. Accordingly, positive affect scales may be especially responsive to the effect of intervention [17].

The current study investigated the role of positive affect in the clinical course of CAD patients who received percutaneous coronary intervention (PCI) with either a sirolimus-eluting stent (SES) or a bare metal stent (BMS) implantation, as part of the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry [18]. The aim of this study was to compare the impact of positive versus negative affect on the risk of clinical events at 2-year follow-up of these patients.

Methods

Participants

The RESEARCH registry population comprised consecutive patients with CAD treated with PCI with either SES or BMS implantation between October 2001 and October 2002 [18]. This registry was designed to evaluate the efficacy and safety of SES implantation in patients treated with PCI in the 'real world' of interventional cardiology; no patients were excluded based on anatomical/clinical presentations, and 68% of the RESEARCH registry patients would not qualify for inclusion in clinical trials [19]. At 6 months post-PCI, all living patients were asked to complete a psychological questionnaire; 874 (71%) returned this questionnaire [20]. Nonresponders were younger, more likely to have a history of MI, to have diabetes and to be treated with ACE inhibitors, but less likely to have renal impairment or to be treated with β-blockers and aspirin than responders (all $P < 0.05$). The mean age of the present sample of 875 patients was 62.2 ± 10.9 years, and 72% ($n = 629$) were men; 41% ($n = 358$) were treated with SES. The study was approved by the local hospital ethics committee, and every patient provided written informed consent.

Symptoms of anxiety and depression

The two seven-item scales of the Hospital Anxiety and Depression Scale (HADS) were administered 6 months post-PCI to assess anxiety and depression symptoms [21].

The HADS has been related to mortality in patients referred for exercise testing; a cut-off score ≥8 yields a good balance between sensitivity and specificity for both scales and was used to indicate probable anxiety and depression caseness [22, 23].

Assessment of positive affect

Self-report depression/anxiety scales not only tap a broad range of negative affects in CAD patients but also (the absence of) positive affect [9]. Previous research in myocardial infarction patients showed that the HADS comprised three distinct factors, and found support for the use of a subscale to assess (the absence of) positive affect [24]. Accordingly, we also used exploratory factor analysis (i.e. principal components analysis with varimax rotation) to examine the notion that positive affect was distinctly different from negative affect in the present study. The scree-plot was used as a criterion for the number of underlying factors to extract.

This analysis yielded two dominant affect factors that were assessed by the HADS measure, and a third, smaller factor. Four items of the HADS reflected a positive affect dimension as indicated by high loadings on factor I; i.e. *being cheerful*, *looking forward with enjoyment to things*, *being still able to enjoy things* and *seeing funny side of things* (Table 1). Corrected item–total correlations ranging between 0.69/0.72 and Cronbach's $\alpha = 0.86$ indicated a high internal consistency of this four-item factor. Previous research supports the use of a factor analytically derived HADS subscale to assess positive affect [24]; by analogy, these four items were summed to comprise a Positive Affect score (range 0–12, mean 9.4, SD 2.9) in this study.

Factor II represented the negative affect dimensions of mood, and was also defined by four items: i.e. *fears something awful will happen* (item 3; factor loading 0.84), *feelings of panic* (item 13; loading 0.83), *frequently worries* (item 5; loading 0.75) and *feels tense* (item 1; loading 0.62). Factor III comprised three items reflecting relaxation; i.e. *not bothered by restlessness* (item 11; loading 0.80), *feels relaxed* (item 7; loading 0.69) and *enjoys a good book or radio/TV program* (item 14; loading 0.67). These items were summed to comprise Negative Affect (mean 3.1 ± 2.8; $\alpha = 0.85$) and Relaxed Affect (mean 6.5 ± 2.1; $\alpha = 0.69$) scores respectively.

Table 1 Positive affect scale ($n = 874$)

Item no.	Factor analysis factor I	Reliability[a] Cronbach's $\alpha = 0.86$	HADS item
1. Looks forward with enjoyment to things	**0.80**	0.69	HADS #12
2. Still enjoys things he/she used to enjoy	**0.79**	0.72	HADS #2
3. He/she can laugh and see funny side	**0.77**	0.72	HADS #4
4. Feels cheerful	**0.74**	0.69	HADS #6

HADS, Hospital Anxiety and Depression Scale [21–23]. Factor loadings are presented in bold.
[a]Corrected item–total correlations; Cronbach's α = estimate of internal consistency.

Two of the three remaining HADS items loaded on the Positive Affect (items 8 and 10) and one on the Negative Affect (item 9) factor. These items had relatively lower item–total correlations, did not add significantly to the internal consistency of the corresponding scales and therefore were not included in the new affect subscales. Overall, we replicated the three-factor model of the HADS, but the Positive Affect subscale that we derived included four items, and not seven as previously described [24].

Endpoint

The endpoint was a composite of death and MI 2 years post-PCI. Events occurring between PCI and psychological assessment were excluded as an endpoint from analyses. MI was diagnosed by a rise in the creatine kinase-MB level to more than three times the upper normal limit [25].

Demographic, clinical variables and medication

Demographic variables included age and sex. Information on clinical variables was obtained from the patients' medical records at the time of psychological assessment. Clinical variables included stent type, multi-vessel disease (52%, $n = 458$), MI (37%, $n = 327$), coronary artery bypass graft (CABG) surgery (12%, $n = 101$) or PCI (25%, $n = 219$) prior to index event, hypercholesterolaemia (81%, $n = 709$), hypertension (39%, $n = 339$), smoking (31%, $n = 273$), renal impairment (creatinine ≤60 ml/min, 30%, $n = 265$) and diabetes (15%, $n = 127$). More than 95% of the patients were treated with β-blockers ($n = 856$), aspirin ($n = 840$) and clopidogrel ($n = 830$); statins (67%), calcium antagonists (47%) and ACE-inhibitors (26%) were also included.

Statistical analyses

Cox regression analyses were performed to investigate continuous scores on the positive affect, negative

affect, depression and anxiety scales as predictors of clinical events. To enhance the clinical interpretability of findings on the role of affect measures in prognosis, similar analyses were used to examine the effect of a 1 SD decrease in positive affect on the clinical course following implantation of coronary stents. Hence, a score ≤7 (i.e. 1 SD below the mean Positive Affect score) was used to identify patients with anhedonia, which refers to markedly reduced positive affect [24]. In multivariable analyses, we adjusted for age, gender and clinical variables. All variables, including reduced positive affect, were entered simultaneously in the multivariable models. In *post hoc* analyses, diabetes and reduced positive affect were used to stratify patients by four risk groups. All statistical tests were two-tailed; $P < 0.05$ was used to indicate statistical significance. Hazard ratios (HR) with 95% confidence intervals (CI) are reported. Analyses were performed using SPSS (SPSS Inc., Chicago, IL, USA) for Windows version 12.0.

Results

Positive affect, depression, anxiety and clinical events

At 2-year follow-up, there were 52 clinical events (death $n = 27$, MI $n = 25$). In univariable analyses, higher scores of positive affect and relaxed affect were associated with a lower risk of clinical events (HR = 0.86 and 0.87 respectively), while higher scores of negative affect (HR = 1.14), depression (HR = 1.10) and anxiety (HR = 1.10) were associated with a higher risk of events (Table 2, top). However, a multivariable regression analysis indicated that positive affect (HR = 0.85), older age (HR = 1.94) and male sex (HR = 2.81) were the only independent predictors of clinical events, and that symptoms of depression, anxiety or other affect measures did not add significantly to this prediction model (Table 2, bottom).

Individual positive affect items and clinical events

To better understand which characteristics of positive affect were responsible for the observed health effect, we examined the relation between individual items and prognosis. The items *being still able to enjoy things* (HR = 0.51, 95% CI 0.40–0.66, $P < 0.0001$), *being cheerful* (HR = 0.62, 95% CI 0.47–0.80, $P < 0.0001$) and *looking forward with enjoyment to things* (HR = 0.66, 95% CI 0.51–0.86, $P = 0.002$) were significantly related to prognosis, adjusting for age and sex. There was a trend for the item *seeing funny side of things* (HR = 0.74, 95% CI 0.55–1.00, $P = 0.053$).

Table 2 Baseline emotions and death/MI post-PCI ($n = 52/874$)

	Hazard ratio [95% CI]	*P*
Univariable analysis		
Affect measures		
Positive affect	0.86 [0.79–0.93]	0.0001
Relaxed affect	0.87 [0.77–0.98]	0.021
Negative affect	1.14 [1.05–1.24]	0.002
HADS Scales		
Depression	1.10 [1.04–1.17]	0.001
Anxiety	1.10 [1.04–1.18]	0.002
Multivariable analysis		
Significant		
Positive affect	0.85 [0.78–0.92]	0.0001
Age ≥60 years	1.94 [1.07–3.54]	0.03
Male sex	2.81 [1.33–5.91]	0.007
Not significant		
Relaxed affect		0.54
Negative affect		0.06
Depression		0.81
Anxiety		0.06

MI, myocardial infarction; PCI, percutaneous coronary intervention.

Reduced positive affect and clinical events

Using a score ≤7 (i.e. 1 SD below the mean) as a cut-off, 211 patients (24%) were classified as experiencing reduced positive affect. These patients had a significantly increased rate of 2-year clinical events (23/211 = 11%) when compared with patients with an adequate positive affect (29/663 = 4%); OR=2.84, 95% CI 1.59–5.07, $P < 0.0001$, adjusted for age and sex. Conversely, a high positive affect score (i.e. 1 SD above the mean) was associated with a decreased risk of clinical events (OR = 0.33, 95% CI 0.15–0.72, $P = 0.005$). However, a multivariable model only retained reduced positive affect as

independent predictor of events ($P < 0.0001$). There was a trend for high positive affect ($P = 0.064$).

Demographic and clinical predictors

In univariable analysis, multi-vessel disease ($P = 0.045$), previous CABG ($P = 0.005$), diabetes mellitus ($P = 0.008$) and ACE-inhibitor therapy ($P = 0.032$) were significantly related to an increased risk of death/MI at 2-years follow-up (Table 3, top). There was also a trend for age ≥60 years ($P = 0.055$), male sex ($P = 0.069$) and previous MI ($P = 0.069$). In multivariable analysis, diabetes mellitus (HR = 2.42), previous CABG (HR = 2.36), male sex (HR = 2.28) and age ≥60 (HR = 2.03) emerged as independent predictors of prognosis (Table 3, bottom); there was a trend for smoking ($P = 0.057$). These variables were included in the following analyses.

The prevalence of reduced positive affect was different as a function of demographic characteristics; i.e. this prevalence was significantly lower in men when compared with women (Table 4). There was also a trend for older age to be associated with reduced positive affect ($P = 0.081$). However, reduced positive affect was not significantly associated with smoking, previous CABG or diabetes.

Independent predictors of cardiac events

To determine whether reduced positive affect and the clinical variables that emerged from previous analyses were independent predictors of prognosis, we entered these factors in a multivariable regression model. The final Cox regression model indicated that reduced positive affect was associated with a more than 150% increase in risk of clinical events, adjusting for clinical and demographic variables (Table 5). Diabetes, previous CABG, male sex and older age (all with an increase in risk >100%) were also independent predictors of events in this regression model.

Diabetes and reduced positive affect subgroups

Because diabetes and reduced positive affect emerged as two independent predictors of clinical

Table 3 Baseline characteristics and death/MI post-PCI (n = 52/874)

	Hazard ratio [95% CI]	*P*
(a) **Univariable analysis**		
Demographics		
Age ≥60 years	1.78 [0.99–3.21]	0.055
Male sex	1.95 [0.95–4.00]	0.069
Clinical factors		
Sirolimus-eluting stent	1.50 [0.83–2.70]	0.18
Multi-vessel disease	1.80 [1.01–3.18]	0.045
Previous MI	1.66 [0.96–2.85]	0.069
Previous CABG	2.54 [1.33–4.83]	0.005
Previous PCI	1.55 [0.87–2.77]	0.014
Hypercholesterolemia	0.84 [0.43–1.63]	0.60
Hypertension	1.17 [0.68–2.03]	0.58
Smoking	1.38 [0.79–2.41]	0.26
Diabetes mellitus	2.29 [1.24–4.24]	0.008
Renal impairment	1.22 [0.69–2.14]	0.50
Beta-blockers	1.10 [0.15–7.96]	0.93
Aspirin	1.04 [0.25–4.29]	0.95
Clopidogrel	2.92 [0.40–21.09]	0.29
Statins	1.06 [0.59–1.92]	0.84
Calcium antagonists	1.28 [0.74–2.22]	0.37
ACE-inhibitors	1.85 [1.06–3.23]	0.032
(b) **Multivariable analysis**		
Age ≥60 years	2.03 [1.10–3.78]	0.024
Male sex	2.28 [1.10–4.73]	0.027
Previous CABG	2.36 [1.21–4.58]	0.011
Smoking	1.76 [0.98–3.15]	0.057
Diabetes mellitus	2.42 [1.31–4.49]	0.005

Previous, prior to index event; MI, myocardial infarction; CABG, coronary artery bypass surgery; PCI, percutaneous coronary intervention.

Table 4 Association between baseline characteristics and reduced positive affect

	Adequate positive affect (n = 663)	Reduced positive affect (n = 211)	*P*-value
Age ≥60 years	54% (360)	61% (129)	0.081
Male sex	74% (490)	66% (139)	0.024
Previous CABG	11% (72)	14% (29)	0.25
Smoking	30% (199)	35% (74)	0.17
Diabetes mellitus	14% (91)	17% (36)	0.23

Number of subjects appears within parentheses.

events, we examined the combination of these factors in relation to prognosis in *post hoc* analyses. Patients were stratified by four subgroups: no diabetes and adequate positive affect ($n = 572$), diabetes but adequate positive affect ($n = 91$), reduced positive affect but no diabetes ($n = 175$) and both diabetes and reduced positive affect ($n = 36$). Patients with no diabetes but reduced positive affect had a similar risk of clinical events when compared with patients with diabetes but adequate positive affect ($P = 0.81$); the effect of reduced positive affect on prognosis was equal to that of diabetes (Fig. 1). Patients with either diabetes or reduced positive affect had a higher risk when compared with nondiabetic patients with adequate positive affect (HR = 2.84, 95% CI 1.58–5.10). Those with both diabetes and reduced positive affect were in the highest risk group (HR = 5.61, 95% CI 2.25–13.99).

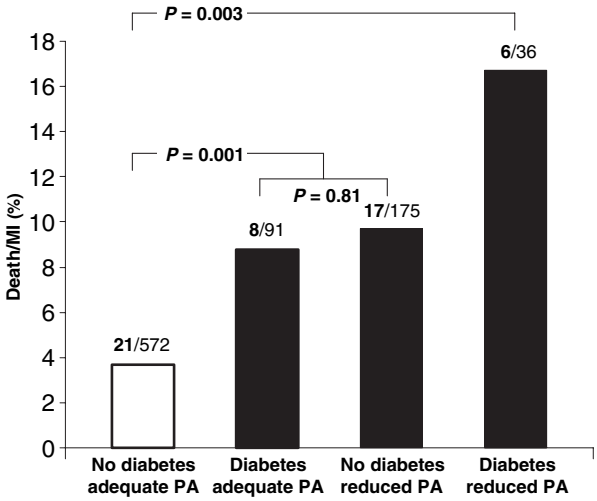

Fig. 1 Clinical events stratified by diabetes/reduced positive affect subgroups. Number of clinical events (bold) and patients are presented on top of each bar. PA: positive affect; adequate PA: score ≥8 on the Positive Affect Scale; reduced PA: score ≤7 on the Positive Affect Scale.

Discussion

The impact of negative emotions has been studied extensively in the context of CAD. By contrast, the potential role of positive emotions on clinical outcome has been neglected. In the current study, we found that the incidence of death/MI 2-year post-PCI was significantly higher in patients with reduced positive affect, with the risk being more than twofold adjusting for demographic and clinical factors. Of note, reduced positive affect was a risk factor on par with diabetes, an established, biomedical risk factor. Stratification of patients by reduced positive affect and diabetes showed that patients with both risk factors had a significantly higher risk compared with the presence of one or neither of these risk factors.

Table 5 Multivariable predictors of death/MI post-PCI ($n = 52/874$)

	Hazard ratio [95% CI]	*P*
Demographics		
Age ≥60 years	2.04 [1.09–3.82]	0.026
Male sex	2.53 [1.21–5.30]	0.014
Clinical factors		
Previous CABG	2.15 [1.11–4.19]	0.024
Smoking	1.62 [0.90–2.91]	0.11
Diabetes mellitus	2.32 [1.25–4.30]	0.008
Psychological status		
Reduced positive affect[a]	2.55 [1.46–4.34]	0.001

Previous, prior to index event; MI, myocardial infarction; CABG, coronary artery bypass surgery; PCI, percutaneous coronary intervention.
[a]Score ≤7 on the Positive Affect Scale coded as 1.

Unresolved issues in coronary-artery stenting include the adverse effect of diabetes on the clinical course post-PCI [26]. The present findings confirm this, but also suggest that markedly reduced positive affect may have an adverse effect as well. Constructs that are related to positive affect such as positive self-perceptions [27] and emotional well-being [28] have previously been associated with increased longevity in older community-dwelling individuals, and optimism has been related to a significantly reduced risk for cardiac events [29]. There is also some evidence to suggest that the relative lack of positive emotions may be a better predictor of clinical outcomes than negative emotions [13, 14, 28]. Accordingly, we also found that the presence of negative emotions, in addition to reduced positive affect,

did not increase the level of prediction of clinical events. These findings suggest that future research should focus more on the role of anhedonia, as indicated by the relative inability to enjoy things or to be cheerful, in the prognosis of CAD patients.

CAD patients may be more likely to recognize themselves by means of a combination of negative and positive emotions rather than negative emotions alone. Positive affect is not merely the opposite of negative affect [6]; rather there seems to be a relative independence of positive and negative affect in CAD patients [8, 10], which the factor analysis of the HADS in the present study also confirmed. Hence, positive affect needs to be assessed in its own right. For example, future randomized trials may benefit from the assessment of basal positive affect levels.

There are several potential pathways through which positive affect could influence health, although at this point they remain speculative as they are yet to be tested empirically. One pathway is health-related behaviours, that is the adoption of more health-promoting practices, such as exercising or getting sufficient sleep [5]. The autonomic nervous system comprises another mechanism, with positive affect probably altering the activity of the sympathetic nervous system in turn leading to decreases in heart rate and blood pressure [5, 12]. The hypothalamus–pituitary–adrenal axis may also be involved, as induction of positive mood states has been shown to lead to reduction in cortisol levels [5]. In turn, cortisol regulation is important in immune functioning. In a recent study, Steptoe *et al.* showed that happiness was inversely related to inflammation, heart rate (although in men only) and cortisol levels [10]. These factors have all been associated with cardiovascular prognosis.

This study has several limitations regarding the causality and conclusiveness of its findings. First, the psychological questionnaires were administered 6 months after stenting because of logistic reasons [20]. This may have biased our results; i.e. there may have been a number of high positive affect individuals who died in the first months post-PCI, before the assessment of positive affect took place. It is also possible that patients who reported more positive affect at this time point were doing so because they had less recurrence of angina or other health problems following successful PCI. However, the study did not include a measure of symptoms at 6 months after stenting, making it impossible to control for the effect of cardiac symptoms at this point in time. Secondly, nonresponders differed from responders on baseline characteristics, and therefore the results may not be generalizable to the total sample. Thirdly, we did not have information on the cause of death, and the combined endpoint included MI as well as all types of death. Fourthly, we had no information on health-related behaviours, apart from smoking, that potentially may explain the relation between affect and health outcome.

Finally, the scale used in this study may not be a typical measure of positive affect; i.e. it includes one affective item (cheerful), two items reflecting the ability to enjoy things (or lack of anhedonia) and one on humour. Nevertheless, the technique that we used to construct a positive affect measure has also been used by others in studies that have factor analysed the Center for Epidemiologic Studies Depression Scale (CES-D) to derive a positive affect component.

This study also has a number of strengths, including its prospective design and use of psychometrically sound measures of self-reported symptoms of depression and anxiety. Moreover, this study was conducted in the 'real world' of interventional cardiology, representing patients seen in daily clinical practice [19]. Research conducted in the 'real world' has been proposed as a means by which to close the gap between research and clinical practice [30]. Finally, given the paucity of research on positive affect and coronary health, the findings of the present study add to our understanding of the influence of emotions on cardiovascular health.

In conclusion, we found that reduced positive affect was a significant independent predictor of adverse clinical events, adjusting for demographic and clinical risk factors. Of note, negative emotions did not

add to the level of prediction of clinical events above and beyond positive emotions and demographic and clinical risk factors. In addition, reduced positive affect was a risk factor on par with diabetes, with patients with both risk factors forming a high-risk group. The present results highlight the importance of looking beyond depression and other negative emotions and also focusing on the relative lack of positive emotions in CAD research and clinical practice. The results also suggest that subgroups of patients, such as those with diabetes and reduced positive affect, may not benefit from coronary-artery stent implantation on par with other patients. Finally, this points to a new target for behavioural interventions, namely focusing on enhancing positive affect.

Conflict of interest statement

No conflict of interest was declared.

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References

1 Rosengren A, Hawken S, Ounpuu S *et al.* Associations of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13468 controls from 52 countries (the INTERHEART study): case–control study. *Lancet* 2004; 364: 953–62.
2 Wang HX, Leineweber C, Kirkeeide R *et al.* Psychosocial stress and atherosclerosis: family and work stress accelerate progression of coronary disease in women. The Stockholm Female Coronary Angiography Study. *J Intern Med* 2007; 261: 245–54.
3 de Jonge P, Spijkerman TA, van den Brink RH, Ormel J. Depression after myocardial infarction is a risk factor for declining health related quality of life and increased disability and cardiac complaints at 12 months. *Heart* 2006; 92: 32–9.
4 Strik JJ, Denollet J, Lousberg R, Honig A. Comparing symptoms of depression and anxiety as predictors of cardiac events and increased health care consumption after myocardial infarction. *J Am Coll Cardiol* 2003; 19: 1801–7.
5 Pressman SD, Cohen S. Does positive affect influence health? *Psychol Bull* 2005; 131: 925–71.
6 Tellegen A, Watson D, Clark LA. On the dimensional and hierarchical structure of affect. *Psychol Sci* 1999; 10: 297–303.
7 Larsen JT, McGraw AP, Cacioppo JT. Can people feel happy and sad at the same time? *J Pers Soc Psychol* 2001; 81: 684–96.
8 Denollet J, De Vries J. Positive and negative affect within the realm of depression, stress and fatigue: the two-factor distress model of the Global Mood Scale (GMS). *J Affect Disord* 2006; 91: 171–80.
9 Denollet J. Emotional distress and fatigue in coronary heart disease: The Global Mood Scale (GMS). *Psychol Med* 1993; 23: 111–21.
10 Steptoe A, Wardle J, Marmot M. Positive affect and health-related neuroendocrine, cardiovascular, and inflammatory processes. *Proc Natl Acad Sci USA* 2005; 102: 6508–12.
11 Lyubomirsky S, King L, Diener E. The benefits of frequent positive affect: does happiness lead to success? *Psychol Bull* 2005; 131: 803–55.
12 Rozanski A, Kubzansky LD. Psychological functioning and physical health: a paradigm of flexibility. *Psychosom Med* 2005; 67: S47–53.
13 Blazer DG, Hybels CF. What symptoms of depression predict mortality in community-dwelling elders? *J Am Geriatr Soc* 2004; 52: 2052–6.
14 Ostir GV, Markides KS, Peek MK, Goodwin JS. The association between emotional well-being and the incidence of stroke in older adults. *Psychosom Med* 2001; 63: 210–5.
15 Moskowitz JT. Positive affect predicts lower risk of AIDS mortality. *Psychosom Med* 2003; 65: 620–6.
16 Chocron S, Etievent JP, Viel JF *et al.* Preoperative quality of life as a predictive factor of 3-year survival after open heart operations. *Ann Thorac Surg* 2000; 69: 722–7.
17 Hevey D, McGee HM, Horgan J. Responsiveness of health-related quality of life outcome measures in cardiac rehabilitation: comparison of cardiac rehabilitation outcome measures. *J Consult Clin Psychol* 2004; 72: 1175–80.
18 Lemos PA, Serruys PW, van Domburg RT *et al.* Unrestricted utilization of sirolimus-eluting stents compared to conventional bare metal stent implantation in the "real world". The Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry. *Circulation* 2004; 109: 190–5.
19 Lemos PA, Serruys PW, van Domburg RT. Sirolimus-eluting stents in the 'real world': the RESEARCH registry rationale and study design. In: Serruys PW, Lemos PA, eds. *Sirolimus-eluting Stents: From RESEARCH to Clinical Practice*. London: Taylor & Francis, 2005; 17.
20 Pedersen SS, Lemos PA, van Vooren PR *et al.* Type D personality predicts death or myocardial infarction after bare metal stent or sirolimus-eluting stent implantation: a Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry sub-study. *J Am Coll Cardiol* 2004; 44: 997–1001.
21 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; 67: 361–70.

22 Herrmann C, Brand-Driehorst S, Buss U, Ruger U. Effects of anxiety and depression on 5-year mortality in 5,057 patients referred for exercise testing. *J Psychosom Res* 2000; 48: 455–62.
23 Bjelland I, Dahl AA, Haug TT, Neckelman D. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. *J Psychosom Res* 2002; 52: 69–77.
24 Martin CR, Lewin RJ, Thompson DR. A confirmatory factor analysis of the Hospital Anxiety and Depression Scale in coronary care patients following acute myocardial infarction. *Psychiatry Res* 2003; 120: 85–94.
25 Smith SC Jr , Dove JT, Jacobs AK *et al.* A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). *J Am Coll Cardiol* 2001; 37: 2215–39.
26 Serruys PW, Kutryk MJ, Ong ATL. Coronary-artery stents. *N Engl J Med* 2006; 354: 483–95.
27 Levy BR, Slade MD, Kunkel SR, Kasl SV. Longevity increased by positive self-perceptions of aging. *J Pers Soc Psychol* 2002; 83: 261–70.
28 Ostir GV, Markides KS, Black SA, Goodwin JS. Emotional well-being predicts subsequent functional independence and survival. *J Am Geriatr Soc* 2000; 48: 473–8.
29 Kubzansky LD, Sparrow D, Vokonas P, Kawachi I. Is the glass half empty or half full? A prospective study of optimism and coronary heart disease in the Normative Aging Study. *Psychosom Med* 2001; 63: 910–6.
30 Krumholz HM, Peterson ED, Ayanian JZ *et al.* Report of the National Heart, Lung, and Blood Institute Working Group on Outcomes Research in Cardiovascular Disease. *Circulation* 2005; 111: 3158–66.

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