

Tilburg University

A general propensity to psychological distress affects cardiovascular outcomes evidence from research on the Type D (Distressed) Personality Profile

Denollet, J.; Schiffer, A.A.J.; Spek, V.R.M.

Published in:
Circulation. Cardiovascular Quality and Outcomes

DOI:
[10.1161/CIRCOUTCOMES.109.934406](https://doi.org/10.1161/CIRCOUTCOMES.109.934406)

Publication date:
2010

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

[Link to publication in Tilburg University Research Portal](#)

Citation for published version (APA):
Denollet, J., Schiffer, A. A. J., & Spek, V. R. M. (2010). A general propensity to psychological distress affects cardiovascular outcomes evidence from research on the Type D (Distressed) Personality Profile. *Circulation. Cardiovascular Quality and Outcomes*, 3(5), 546-557. <https://doi.org/10.1161/CIRCOUTCOMES.109.934406>

General rights

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

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

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Circulation

Cardiovascular Quality and Outcomes

American Heart Association 

Learn and Live

JOURNAL OF THE AMERICAN HEART ASSOCIATION

A General Propensity to Psychological Distress Affects Cardiovascular Outcomes: Evidence From Research on the Type D (Distressed) Personality Profile

Johan Denollet, Angélique A. Schiffer and Viola Spek

Circ Cardiovasc Qual Outcomes 2010;3;546-557

DOI: 10.1161/CIRCOUTCOMES.109.934406

Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75254

Copyright © 2010 American Heart Association. All rights reserved. Print ISSN: 1941-7705. Online ISSN: 1941-7713

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

<http://circoutcomes.ahajournals.org/cgi/content/full/3/5/546>

Subscriptions: Information about subscribing to *Circulation: Cardiovascular Quality and Outcomes* is online at

<http://circoutcomes.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax: 410-528-8550. E-mail:

journalpermissions@lww.com

Reprints: Information about reprints can be found online at

<http://www.lww.com/reprints>

A General Propensity to Psychological Distress Affects Cardiovascular Outcomes

Evidence From Research on the Type D (Distressed) Personality Profile

Johan Denollet, PhD; Angélique A. Schiffer, PhD; Viola Spek, PhD

Specific negative emotions have been related to adverse cardiac events, but a general propensity to psychological distress may also affect cardiovascular outcomes. In this summary article, we provide a reliable estimate of the prognostic risk associated with Type D (distressed) personality, a general propensity to distress that is defined by high scores on the “negative affectivity” and “social inhibition” traits. Quantitative analyses of prospective studies that included a total of 6121 patients with a cardiovascular condition indicated that Type D personality was associated with a more than 3-fold increased risk of adverse events (9 studies) and long-term psychological distress (11 studies). In addition, a narrative review of 29 studies showed that Type D personality and depression are distinct manifestations of psychological distress, with different and independent cardiovascular effects. There are also plausible biological and behavioral pathways that may explain this adverse effect of Type D personality. The findings reported in this summary article support the simultaneous use of specific and general measures of distress in cardiovascular research and practice.

General Propensity to Distress

Depression, anxiety, anger, and posttraumatic stress are specific markers of distress that have been related to cardiac disorder,¹⁻⁵ whereas broader markers of psychological distress have received substantially less attention in cardiovascular research.⁶ However, the general distress shared across these specific markers may predict the development of coronary heart disease¹ and may also partly account for the association of depression and anxiety with myocardial infarction,³ poor cardiac prognosis,⁴ and autonomic cardiac dysregulation.⁷ Hence, the conceptual idea of psychological distress as a cardiovascular risk marker may be broadened to include a general propensity to distress.

Many studies report on depression, anxiety, and cardiovascular outcomes.²⁻⁴ Although patients may go in and out of depressive and anxious episodes, there is an underlying trait factor that predisposes patients to chronic distress.⁸ Symptoms of depression/anxiety not only reflect episodic distress but also a more ingrained tendency to experience distress.^{3,9}

with the combination of distress and social isolation predicting poor cardiac prognosis.^{10,11} Accounting for this general propensity to psychological distress offers the opportunity to flag high-risk patients that may benefit from a more personalized approach to cardiac care. The “distressed” or Type D personality¹²⁻¹⁵ refers to a chronic, more covert form of distress that is distinct from depression. Type D patients are inclined to experience negative emotions (negative affectivity) and to inhibit self-expression in social interaction (social inhibition).¹⁵ Several studies from our research group have examined the notion that Type D personality is a general propensity to psychological distress that affects cardiovascular outcomes.^{16,17} The determinants of psychological distress as a cardiac risk marker¹⁻⁵ are still unclear; hence, a number of these studies also focused on the role of Type D as predictor of distress.

In identifying chronically distressed patients, we can develop new interventions to minimize the adverse consequences of negative emotions on cardiovascular outcomes. To have added value, this general propensity to distress should show a substantial effect on cardiovascular outcomes and should show this effect, irrespective of measures of depression. The purpose of this paper was to summarize the findings from our follow-up research on Type D personality that were published over a 15-year period (between 1995 and 2009). This summary includes both a quantitative synthesis and a narrative review that address 2 issues: (1) What is the increase in prognostic risk associated with Type D personality? and (2) Does this increase in risk withstand adjustment for depression?

Methods

Inclusion of Studies

To provide a reliable estimate of the prognostic risk associated with Type D personality, we performed a quantitative analysis of aggregate findings from our Type D studies that were published between 1995 and 2009. Two of the authors (V.S. and A.S.) and a librarian also searched for Type D studies from other research groups through systematic literature searches in the databases of PubMed and PsychINFO (1995 to 2009). Searches were conducted using the following search terms: “Type D (type-D, Type-D)” AND “cardiovascular disease/cardiac

From the CoRPS—Center of Research on Psychology in Somatic diseases (J.D., A.A.S., V.S.), Tilburg University, Tilburg, The Netherlands; and the Department of Medical Psychology and Neuropsychology (A.A.S.), TweeSteden Hospital, Tilburg, The Netherlands.

Correspondence to Johan Denollet, PhD, CoRPS, Department of Medical Psychology, Tilburg University, PO Box 90153, 5000 LE Tilburg, The Netherlands. E-mail denollet@uvt.nl

(*Circ Cardiovasc Qual Outcomes*. 2010;3:546-557.)

© 2010 American Heart Association, Inc.

Circ Cardiovasc Qual Outcomes is available at <http://circoutcomes.ahajournals.org>

DOI: 10.1161/CIRCOUTCOMES.109.934406

disease/coronary heart disease/myocardial infarction"; "Type D (type-D/Type-D)" AND "cardiovascular disease/cardiac disease/coronary heart disease/myocardial infarction" AND "depression/depressive symptoms." We also checked reference lists of retrieved studies and of 2 earlier narrative reviews on Type D.^{16,17}

The following criteria were used to select prognostic studies on Type D personality: (1) the study focuses on Type D personality in relation to hard medical outcomes (ie, death or recurrent MI) or emotional distress (ie, depression, anxiety and poor mental health status); (2) the study uses a prospective design; (3) the study was conducted in a cardiovascular population; (4) the study reports multivariable odds ratios that adjust for disease severity; and (5) when there was an overlap between samples across studies, only 1 of these studies was included. The retrieved studies were independently assessed (by A.S. and V.S.) on the above-mentioned inclusion criteria. The degree of agreement on the selection of prognostic studies was high; there was only disagreement on studies of patients with peripheral arterial disease, but, eventually, these studies were included in the analyses. The systematic literature searches did not yield prognostic Type D studies from other research groups, and we are not aware of any unpublished negative studies by others.

Quantitative Synthesis of Aggregate Findings

Meta-analytic reports usually combine studies from diverse sources of research groups; hence, the current quantitative analysis that aggregated findings from our own research group should not be regarded as a meta-analysis in a standard way. However, given the fact that there is some disparity in data from our published reports, as indicated by a wide range in odds ratios and confidence intervals of the individual reports, the purpose of this summary article was to reliably estimate the risk associated with Type D personality in our research on cardiovascular patients and to enhance interpretation of published reports.

The fact that all studies included in the quantitative synthesis originated from our own group clearly precludes an independent rating of the quality of the studies; hence, we did not check the quality of reporting of our own research. However, the second and last author (A.S. was involved in 3 studies; V.S. was not involved in any study) used the 14-item rating of the "Methods and Results" part of the STROBE criteria^{18,19} to provide an indication of the methodological quality of the studies. The mean score for methodological quality was 12.9 (of 14); the most common methodological problem was the absence of an a priori power calculation. Regarding the quality of the individual reports, it should be noted that the prognostic studies were published in well respected journals and that all papers have been scrutinized by scrupulous and dedicated reviewers before being accepted for publication.

The computer program Comprehensive Meta-analysis, version 2.2.021 (Biostat, Englewood, NJ) was used to calculate pooled mean odds ratios. Because we did not know whether we could expect heterogeneity across studies, both fixed- and random-effects models were used to calculate the pooled effect size. Heterogeneity was calculated with the Q -statistic and the I^2 -statistic. A significant Q indicates that the variability among the effect sizes is greater than what is likely to have resulted from subject-level sampling error alone.²⁰ I^2 describes the percentage of total variation across studies that is due to heterogeneity rather than chance. I^2 -values of 25%, 50%, and 75% are associated with low, moderate, and high heterogeneity.²¹ Post hoc subgroup analyses included both fixed-effects and mixed-effects analyses. In fixed-effects analyses, the model calculates the fixed-effect sizes for each subgroup of studies-, and for the difference between subgroups. In mixed-effects analyses, the random-effects model calculates the effect size for each subgroup, whereas the fixed-effects model examines the difference between subgroups of studies. Separate analyses were conducted for prognosis and distress. Publication bias was estimated visually by funnel plots and by calculating the fail-safe N , the number of nonsignificant studies that would be necessary to reduce the effect size to a nonsignificant value.

Narrative Review of Type D and Depression

The narrative part of this summary article focused on studies that included the assessment of both Type D personality and symptoms/diagnosis of depression. To have added value, the general propensity to psychological distress as defined by the Type D construct should affect cardiovascular disorder, irrespective of established measures of depression.

In addition to studies that reported on (1) conceptual differences between Type D personality and depression; this part of the article also included studies that reported on (2) the independent prognostic power of Type D personality after adjustment for depression, (3) the relation of Type D personality and depression to biological mechanisms of disease, and (4) the role of Type D personality and depression in patient-reported health outcomes. Assessment of depression in these studies was based on standard interview ratings of the diagnosis and severity of depression or validated self-report scales of depressive symptoms. This narrative review of studies that assessed both Type D personality and depression included 23 reports from our own research group and 6 reports from other research groups.

Results

Nineteen studies with 6121 patients were included in quantitative data synthesis of Type D follow-up studies on prognosis (Table 1) and psychological distress (Table 2); there was no overlap in patient samples. There was 1 study that reported on both prognosis and psychological distress.²³ All studies were published between 1996 and 2009.

Type D Personality and Prognosis

Nine prospective Type D studies reported on long-term prognosis, including (cardiac) death, myocardial infarction, and revascularization (Table 1). Six reports on prognosis were published in cardiology journals (*Circulation*,^{23,27} *J Am Coll Cardiol*,²⁵ *Am J Cardiol*,²⁴ *Eur J Cardiovasc Prev Rehabil*,²⁶ and *Int J Cardiol*²⁸) and 3 in other biomedical journals (*Lancet*,²² *J Heart Lung Transplant*,²⁹ and *Arch Surg*³⁰). In patients with coronary heart disease, Type D personality was associated with an odds ratio ≥ 2.5 in 2 studies^{24,26} and an odds ratio ≥ 3.8 in 4 studies.^{22,23,25,27} Type D personality was also associated with an odds ratio ≥ 2.3 in heart failure,²⁸ heart transplantation,²⁹ and peripheral arterial disease.³⁰

There was no significant heterogeneity among these studies on prognosis, ($Q=6.6$, $df=8$, $P<0.001$, $I^2=0.0\%$), indicating that the pooling of studies was warranted.

Examination of the pooled effect size indicated that Type D personality was associated with a more than 3-fold increased risk of poor long-term prognosis (Figure 1). The mean odds ratio of all 9 prospective studies on prognosis was 3.7 (95% confidence interval, 2.7~5.1) in both the fixed-effects and random-effects models (Table 3, top). Publication bias was estimated visually by funnel plots, and the fail-safe N was 151 for studies on cardiac prognosis.

Type D Personality and Emotional Distress

Eleven papers reported on the prediction of emotional distress (anxiety, depression, vital exhaustion, and poor mental health); these studies were published in cardiology,^{23,33,34,38} surgery,^{39,40} and psychiatry^{31,32,35-37} journals (Table 2). In coronary patients, Type D was associated with an odds ratio ≥ 1.9 in 3 studies^{23,34,36} and ≥ 3.0 in 4 studies.^{31-33,35} The odds ratio was ≥ 3.8 in heart failure^{37,38} and peripheral arterial disease^{39,40} patients.

Table 1. Studies on Prognosis, Adjusted for Clinical and Demographic Factors

Selected Study First Author	Journal	Characteristics				Outcomes		
		CVD	N	Type D (n)	FU	Prognosis	OR*	Covariates
Denollet ²² (1996)	<i>Lancet</i>	CAD	303	28% (85)	6–10 years	Cardiac death	OR=3.8	LVEF, multivessel disease, poor exercise tolerance, lack of thrombolytic therapy
Denollet ²³ (2000)	<i>Circulation</i>	CAD	319	31% (99)	5 years	Cardiac death and MI	OR=8.9	LVEF Age
Denollet ²⁴ (2006)	<i>Am J Cardiol</i>	CAD	337	29% (98)	5 years	MACE	OR=2.9	LVEF, index MI, no CABG at baseline Age, sex, psychological stress
Pedersen ²⁵ (2004)	<i>J Am Coll Cardiol</i>	CAD	875	29% (254)	¾ year	Death and MI	OR=5.3	Previous CABG, bare vs drug-eluting stent Age, sex
Pedersen ²⁶ (2007)	<i>Eur J Cardiovasc Prev Rehabil</i>	CAD	358	30% (106)	2 years	Death and MI	OR=2.5	Multivessel disease, cardiac history, hypertension, hypercholesterolemia, diabetes, renal impairment Age, sex, smoking
Denollet ²⁷ (1998)	<i>Circulation</i>	MI	87	31% (27)	6–10 years	Cardiac death and MI	OR=4.8	LVEF, multivessel disease, poor exercise tolerance, history of previous MI Smoking, depression, anxiety, anger
Schiffer ²⁸ (2010)	<i>Int J Cardiol</i>	CHF	232	21% (48)	2.6 years	Cardiac death	OR=2.3	LVEF Age, sex
Denollet ²⁹ (2007)	<i>J Heart Lung Transplant</i>	HTx	51	29% (15)	5.4 years	Death, severe/early allograft rejection	OR=6.8	Donor (age, brain death), recipient (CMV+, diabetes, creatinine, hypertension, BMI), mismatch (female-to-male, HLA, CMV), allograft type, urgent transplantation Age, sex
Aquarius ³⁰ (2009)	<i>Arch Surg</i>	PAD	184	35% (64)	4 years	Death	OR=3.5	Ankle-brachial index, diabetes, renal disease, pulmonary disease Age, sex

*All odds ratios are multivariably adjusted; covariates are stated in the column on the far right.

BMI indicates body mass index; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; CHF, chronic heart failure; CMV, cytomegalovirus; CVD, cardiovascular disease; FU, follow-up; HTx, heart transplantation; LVEF, left ventricular ejection fraction; MACE, major adverse cardiac event; MI, myocardial infarction; OR, odds ratio; and PAD, peripheral arterial disease.

The fixed-effects (odds ratio=3.2) and random-effects (odds ratio=3.4) models yielded slightly different results (Figure 2). There was significant heterogeneity (Table 3; $Q=13.76$). Therefore, post hoc analyses were performed for cardiac and peripheral arterial disease subgroups. In cardiac patients, the mean odds ratio was 2.9 for both models, and heterogeneity was much lower than in the total sample (Table 3; subgroups distress). In the subgroup of patients with peripheral arterial disease, the mean odds ratio was 7.0 for both models, and there was no significant heterogeneity (Table 3; subgroups distress). Publication bias was estimated visually by funnel plots and by calculating the fail-safe N, which was 346 for studies on emotional distress.

Studies Excluded From Quantitative Analysis

Three publications on Type D personality and prognosis that were published between 1995 and 2008 (*Psychosom Med*,¹⁴ *Eur Heart J*,⁴¹ and *Arch Intern Med*⁴²) were excluded from quantitative analysis because of overlap with samples of 3

other published papers.^{22,24,25} One study showed that the combination of social inhibition and negative affectivity (rather than the isolated effect of 1 of these traits) was associated with adverse events after coronary stenting⁴¹ and another that Type D personality was independently associated with adverse events in coronary patients, after adjustment for depressive symptoms.⁴²

Narrative Review of Type D Personality and Depression

Twenty-nine studies reported on both Type D personality and depression in cardiovascular patients (Table 4). Eleven studies were published in cardiology journals,^{23,27,33,38,41,47,52,56–59} 2 in general medicine,^{22,42} and 16 in psychiatry/psychology.^{35–37,43–46,48–51,53–55,60,61}

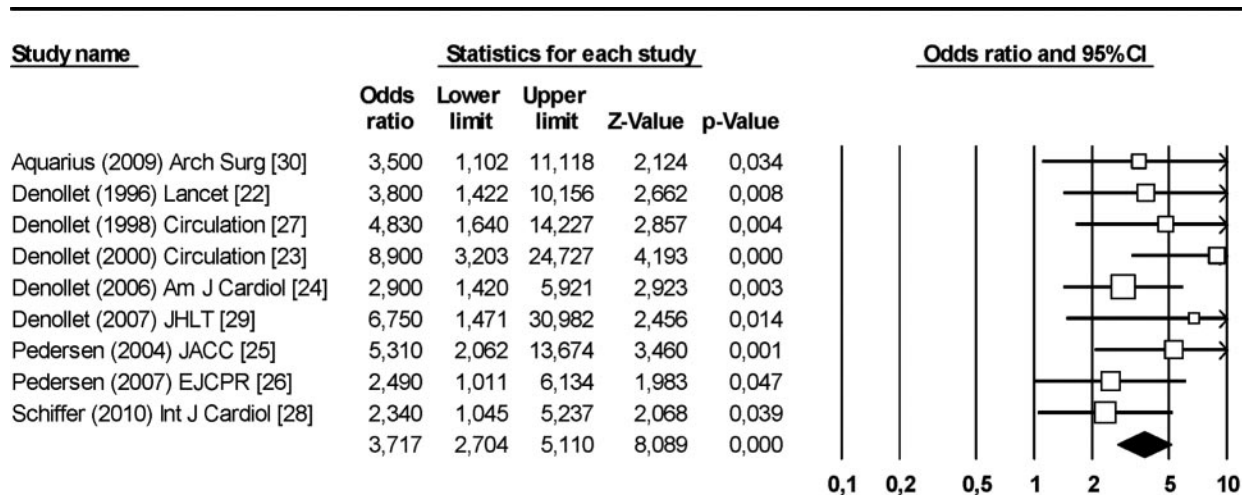
The Composite International Diagnostic Interview (CIDI)^{43,50} or Hamilton Depression rating scale⁴⁹ was used in 3 studies to assess clinical depression. Most studies used the Beck Depression Inventory (BDI),^{37,38, 42,44,45,48,52–58,61} Hospital Anxiety and

Table 2. Studies on Psychological Distress, Adjusted for Clinical and Demographic Factors

Selected Study First Author	Journal	Characteristics				Outcomes		
		CVD	N	Type D (n)	FU	Emotional Distress	OR*	Covariates
Denollet ²³ (2000)	<i>Circulation</i>	CAD	319	31% (99)	5 years	Depressive affect (GMS, NA+/PA-)	OR=2.6	Sex, smoking, depression, anxiety
Pedersen ³¹ (2001)	<i>J Psychosom Res</i>	CAD	171	29% (49)	6 weeks	Vital exhaustion (MQ ≥ 14)	OR=4.7	NYHA class, cardiac treatment Age, sex, education, marital status, work status
Pedersen ³² (2007)	<i>J Psychosom Res</i>	CAD	419	25% (104)	1 year	Vital exhaustion (MQ ≥ 14)	OR=3.5	Multivessel disease, unstable angina, drug-eluting stent, cardiac history, hypertension, dyslipidemia, diabetes Age, sex, smoking, baseline exhaustion
Pedersen ³³ (2006)	<i>Am Heart J</i>	CAD	542	17% (94)	½ year	Depressive symptoms (HADS-D ≥ 8)	OR=3.0	Multivessel disease, stent type, diabetes Age, sex
Pedersen ³⁴ (2007)	<i>Int J Cardiol</i>	CAD	692	27% (190)	1 year	Poor mental health (SF-36 low tertile)	OR=1.9	Multivessel disease, cardiac history, recent event, hypertension, dyslipidemia, diabetes, renal impairment Age, sex, SES, smoking, baseline health status
Spindler ³⁵ (2007)	<i>J Affect Disorders</i>	CAD	167	59% (98)	½ year	Anxiety symptoms (HADS-A ≥ 8)	OR=3.3	Multivessel disease, drug-eluting stent, cardiac history, hypertension, dyslipidemia, diabetes, renal impairment Age, sex, smoking, depression
van Gestel ³⁶ (2007)	<i>J Affect Disorders</i>	CAD	416	25% (103)	1 year	Anxiety symptoms (HADS-A ≥ 8)	OR=2.9	Multivessel disease, unstable angina, cardiac history, recent event, hypertension, dyslipidemia, diabetes Age, sex, living alone, smoking, depression, baseline anxiety
Schiffer ³⁷ (2008)	<i>J Affect Disorders</i>	CHF	149	23% (35)	1 year	Anxiety [mild/severe] (HAM-A ≥ 17)	OR=5.3	LVEF, NYHA class, ischemia, hypertension Age, sex, education, partner status, smoking, depression, anxiety sensitivity
Schiffer ³⁸ (2008)	<i>Eur J Heart Failure</i>	CHF	166	23% (38)	1 year	Poor mental health (SF-36, low tertile)	OR=3.8	LVEF, NYHA class, diuretics, nitrates, ACE inhibitors, β -blockers, spironolactone, psychotropic medication Age, sex, education, baseline mental health status
Aquarius ³⁹ (2007)	<i>J Vasc Surg</i>	PAD	203	34% (69)	1 year	Poor mental health (RAND, low quartile)	OR=6.0	Ankle-brachial index, claudication distance Age, sex
Aquarius ⁴⁰ (2007)	<i>Arch Surg</i>	PAD	150	35% (52)	½ year	Depressive symptoms (10-item CES-D ≥ 4)	OR=8.6	Ankle-brachial index, walking distance (pain free, maximum), comorbid disease (carotid, cardiac, renal, pulmonary), hypertension, hyperlipidemia, diabetes Age, sex, smoking

*All odds ratios are multivariably adjusted; covariates are stated in the column on the far right.

ACE indicates angiotensin-converting enzyme; CAD, coronary artery disease; CES-D, Center for Epidemiological Studies Depression Scale (10-item Boston form); CHF, chronic heart failure; CVD, cardiovascular disease; FU, follow-up; GMS, Global Mood Scale (NA+/PA-: high negative affect paired with low positive affect as defined by median split); HADS, Hospital Anxiety and Depression Scale; HAM-A, Hamilton Anxiety Rating Scale; LVEF, left ventricular ejection fraction; MQ, Maastricht Questionnaire; NYHA, New York Heart Association; OR, odds ratio; PAD, peripheral arterial disease; RAND, RAND-36 mental health domains; SES, socioeconomic status; and SF-36, Short-Form Health Survey-36.



Meta Analysis

Figure 1. Meta-analysis of Type D personality and prognosis. Note: All odds ratios were multivariably adjusted (see Table 1). EJCPR indicates *Eur J Cardiovasc Prev Rehabil*; JACC, *J Am Coll Cardiol*; and JHLT, *J Heart Lung Transplant*.

Depression Scale (HADS),^{33,35,36,41,44,46,51,59,60} or other self-report measures^{22,23,27,47} of depressive symptoms. This review included 8 studies that reported on conceptual differences,^{33,42–48} 6 studies on the prediction of adverse events,^{22,23,27,41,42,49} 6 studies on biological mechanisms of disease,^{50–55} and 10 studies on perceived health status and anxiety.^{35–38,56–61}

Overlap Between Type D personality and Depression

From a conceptual point of view, evidence indicates that Type D personality and depression are only partly overlapping. Most Type D patients do not cross the diagnostic threshold for clinical depression,⁴³ and similar findings were found regarding self-reported depression.⁴² Factor analysis including the BDI and HADS depression scales confirmed that the items from the 14-item Type D Scale (DS14)¹⁵ were distinctly different from depressive symptoms in cardiac patients.⁴⁴ In addition, Type D predicted the onset of depressive symptoms in patients who were free from depression at baseline³³ and predicted the prevalence^{46,47} and persistence⁴⁸

of depressive symptoms, adjusting for baseline levels of depression.

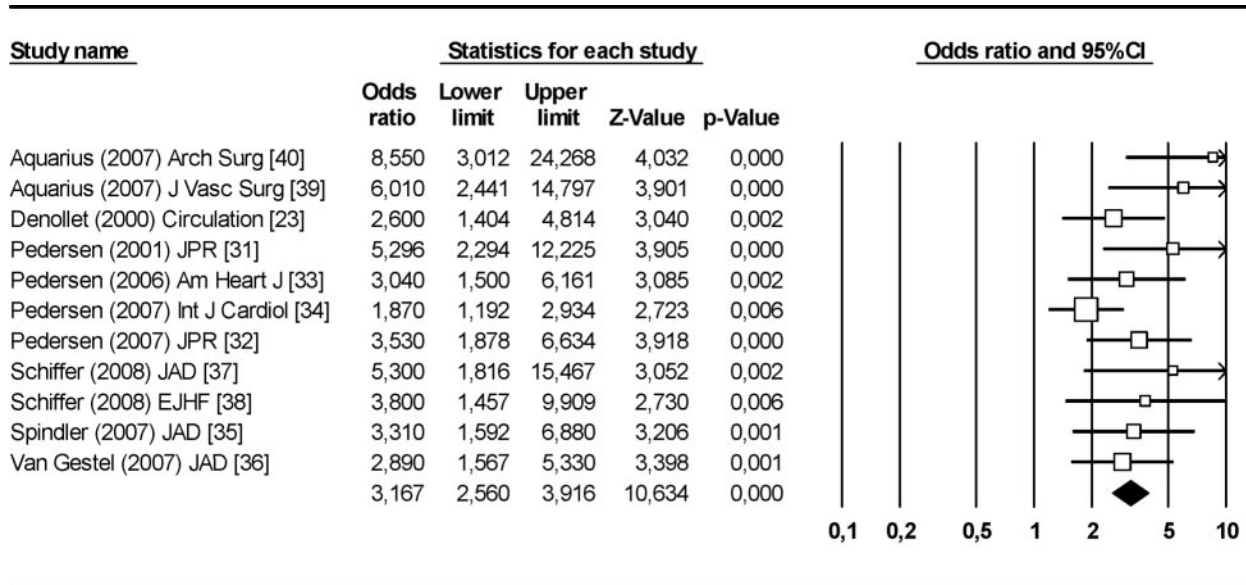
Differences Between Type D Personality and Depression

In 5 follow-up studies of cardiac patients, Type D personality independently predicted adverse cardiac events, adjusting for symptoms^{22,23,27,42} and severity⁴⁹ of depression. In another study, Type D personality but not depressive symptoms predicted adverse events.⁴¹ Although left ventricular dysfunction has been related to an increased risk of depression,⁵⁰ it is less likely that Type D is confounded by the severity of cardiac disorder. Clinical markers of disease severity are not related to Type D personality,^{45,50} and the association between Type D and cardiovascular outcomes remains after adjustment for disease severity (see Table 1). One study reported that depression but not Type D was associated with atrial fibrillation,⁵¹ whereas another study showed that anxious Type D patients were at risk of ventricular arrhythmia and that depressive symptoms were unrelated to arrhythmia.⁵² Three studies in cardiac patients showed that Type

Table 3. Meta-Analyses of Type D Studies on Prognosis and Emotional Distress

	N _{studies}		OR	95% CI	Q	P	I ² (%)
Total group							
Prognosis	9	FEM	3.7	2.7–5.1	6.6	<0.01	0.0
		REM	3.7	2.7–5.1			
Emotional distress	11	FEM	3.2	2.6–3.9	13.76	0.18	27.4
		REM	3.4	2.6–4.3			
Subgroup distress							
Cardiac disease	9	FEA	2.9	2.3–3.6	7.74	0.46	0.0
		MEA	2.9	2.3–3.6			
Peripheral arterial disease	2	FEA	7.0	3.5–13.8	0.25	0.62	0.0
		MEA	7.0	3.5–13.8			

OR indicates odds ratio; CI, confidence interval; FEM, fixed-effects model; REM, random-effects model; FEA, subgroup analysis based on the fixed-effects model; and MEA, subgroup analysis based on the mixed-effects model.



Meta Analysis

Figure 2. Meta-analysis of Type D personality and emotional distress. Note: All odds ratios were multivariably adjusted (see Table 2). JAD indicates *J Affect Disorders*; and JPR, *J Psychosom Res*.

D remained significantly related to increased levels of cortisol^{53,54} and oxidative stress,⁵⁵ after adjustment for depressive symptoms.

In a study of coronary patients, depressive symptoms but not Type D predicted return to work.⁵⁶ In another study, Type D personality but not depression was associated with poor health status 1 year after coronary bypass surgery.⁵⁹ After control for depressive symptoms, Type D personality was also associated with poor health status and fatigue in myocardial infarction⁵⁷ and heart failure^{38,58} patients and in patients who participated in cardiac rehabilitation.⁶⁰ In a study of patients with an acute coronary syndrome, Type D predicted posttraumatic stress symptoms but adjustment for depressive symptoms attenuated this relationship.⁶¹ Finally, Type D personality predicted the prevalence,³⁶ persistence,³⁵ and severity³⁷ of anxiety symptoms in cardiac patients, adjusting for depressive symptoms.

Discussion

Risk Associated With Type D

Individual published reports on Type D personality have yielded some disparity in data as indicated by a wide range in odds ratios and confidence intervals across studies. This summary article provides a more reliable estimate of the increase in risk associated with Type D personality. Quantitative analysis of prospective studies from our group indicated that Type D personality was associated with a more than 3-fold increased risk of poor prognosis, with the 95% confidence interval of this pooled odds ratio ranging from 2.7 to 5.1.

Only multivariable odds ratios that adjusted for demographic and clinical variables were used in quantitative data analysis. Type D personality was also associated with a 3-fold (range, 2.6 to 4.3) increased risk of distress, which enhanced the generalizability of findings. These studies found that Type D personality independently predicted anxiety^{36,37}, poor men-

tal health,^{34,38} and vital exhaustion³² after adjustment for baseline levels of distress. Overall, these findings suggest that general distress affects cardiovascular outcomes.

Type D Is Not Depression

Depression is an episodic risk marker and Type D a chronic risk marker for clinical manifestations of coronary disease.⁸ Although depression reflects a psychiatric disorder, Type D refers to normal personality traits, with most Type D patients not meeting diagnostic criteria for depression.⁴³ Some Type D individuals will only cross the threshold for affective disorder during times of elevated stress, and still others will display subclinical levels of distress all their lives.⁶² Type D and depression are only partly overlapping,^{42,43} and factor analytic research showed that items from the Type D personality scale are different from depressive symptoms.^{44,63}

After adjustment for co-occurring depression symptoms, Type D personality remains independently associated with an increased risk of clinical events.^{22,23,27,41,42,49} This suggests that both constructs involve distinct pathways of disease. Evidence also shows that after control for depressive symptoms, Type D was associated with ventricular arrhythmia,⁵² increased cortisol,^{53,54} and oxidative stress⁵⁵ in cardiac patients. Further, Type D predicted the onset,³³ prevalence,^{36,46,47} persistence,^{35,48} and severity³⁷ of depression and anxiety symptoms in cardiac patients, adjusting for baseline depression scores. In addition, Type D is associated with poor health status and fatigue,^{38,57–60} adjusting for depressive symptoms.

These findings do not imply that Type D is better than depression in the prediction of cardiac outcomes; they simply indicate that general distress may have incremental value. Rather than antonymous perspectives, specific (depression, anxiety) and general (Type D) approaches to distress represent complementary perspectives that have additional value

Table 4. Studies That Included Both Type D Personality and Depression Assessment

First Author and Publication	Patients	Depression Measure	Scale	Findings on Type D and Depression
Conceptual differences				
Denollet ⁴³ (2008) <i>Psychol Med</i>	MI n=1205	Affective disorder	CIDI	224 patients were Type D and 206 had depression; only 90 patients (7%) had both forms of distress
Denollet ⁴² (2008) <i>Arch Intern Med</i>	CAD n=337	Depression symptoms	BDI	43 patients were Type D only and 58 had depression only; 55 patients had both Type D and depression
Pelle ⁴⁴ (2009) <i>J Affect Disord</i>	CAD/CHF n=565	Depression symptoms	BDI HADS	Type D personality traits were distinctly different from depression in factor analysis
Martens ⁴⁵ (2007) <i>J Psychosom Res</i>	MI n=475	Depression symptoms	BDI	Type D classification was not confounded by variability in depressive symptoms over time
Pedersen ³³ (2006) <i>Am Heart J</i>	CAD n=542	Depression symptoms	HADS	Type D predicted onset of depressive symptoms in patients who were free from depression at baseline
Spindler ⁴⁶ (2009) <i>Int J Behav Med</i>	CAD/CHF n=318	Depression symptoms	HADS	Type D independently predicted depression, adjusting for baseline levels of depression
Smith ⁴⁷ (2008) <i>EJCP</i>	CAD/CHF n=506	Depression symptoms	MQ-D	Type D independently predicted depression, adjusting for baseline levels of depression
Martens ⁴⁸ (2008) <i>Psychol Med</i>	MI n=287	Depression symptoms	BDI	Type D independently predicted persistence of depressive symptoms, adjusting for prior depression
Prognostic differences				
Martens ⁴⁹ (2010) <i>J Clin Psychiat</i>	MI n=473	Depression severity	HAM-D	Type D independently predicted cardiac death/MI, after adjustment for severity of depression
Denollet ⁴² (2008) <i>Arch Intern Med</i>	CAD n=337	Depression symptoms	BDI	Type D independently predicted major adverse cardiac events, adjusting for depression
Denollet ⁴¹ (2006) <i>Eur Heart J</i>	CAD n=875	Depression symptoms	HADS	Type D independently predicted major adverse cardiac events; depression was not related to events
Denollet ²² (1996) <i>Lancet</i>	CAD n=303	Pessimism Despair	MBHI	Type D independently predicted cardiac death; depression only significant in univariate model
Denollet ²⁷ (1998) <i>Circulation</i>	MI n=87	Pessimism Despair	MBHI	Type D independently predicted cardiac death/MI; depression only significant in univariate model
Denollet ²³ (2000) <i>Circulation</i>	CAD n=319	Despondency	HPPQ	Type D independently predicted cardiac death/MI; depression only significant in univariate model
Biological differences				
de Jonge ⁵⁰ (2007) <i>J Psychosom Res</i>	MI n=1205	Affective disorder	CIDI	Type D was not associated with disease severity; depression associated with ventricular dysfunction
Lange ⁵¹ (2007) <i>J Psychosom Res</i>	AF n=54	Depression symptoms	HADS	Type D was not associated with atrial fibrillation; depression independently predicted atrial fibrillation
van den Broek ⁵² (2009) <i>J Am Coll Card</i>	ICD n=391	Depression symptoms	BDI	Anxious Type D patients were at risk of ventricular arrhythmias; depression not related to arrhythmia
Whitehead ⁵³ (2007) <i>J Psychosom Res</i>	CAD n=72	Depression symptoms	BDI	Type D was associated with an increased cortisol awakening response, adjusting for depression
Molloy ⁵⁴ (2008) <i>Psychosom Med</i>	CAD n=70	Depression symptoms	BDI	Type D independently predicted increased cortisol levels; depression was not related to cortisol
Kupper ⁵⁵ (2009) <i>Psychosom Med</i>	CHF n=122	Depression symptoms	BDI	Type D was associated with oxidative stress levels; depression was not related to oxidative stress
Differences in health status				
Bhattacharyya ⁵⁶ (2007) <i>Eur Heart J</i>	ACS n=126	Depression symptoms	BDI	Type D not related to returning to work; depression independently predicted failure to resume work
Schiffer ³⁸ (2008) <i>Eur J Heart Fail</i>	CHF n=166	Depression symptoms	BDI	Type D independently predicted poor health status, adjusting for depression
Mols ⁵⁷ (2010) <i>Heart</i>	MI n=503	Depression symptoms	BDI	Type D was associated with poor health status and unstable angina, adjusting for depression
Smith ⁵⁸ (2007) <i>Eur J Heart Fail</i>	CHF n=136	Depression symptoms	BDI	Type D independently predicted symptoms of general fatigue, adjusting for depression
Al-Ruzzeh ⁵⁹ (2005) <i>Heart</i>	CABG n=437	Depression symptoms	HADS	Type D independently predicted poor health status; depression was not associated with health status
Pelle ⁶⁰ (2008) <i>Ann Behav Med</i>	CAD n=368	Depression symptoms	HADS	Type D independently predicted poor health status before and after rehabilitation, adjusting for depression

(Continued)

Table 4. Continued

First Author and Publication	Patients	Depression Measure	Scale	Findings on Type D and Depression
Differences in anxiety				
Spindler ³⁵ (2007) <i>J Affect Disord</i>	CAD n=167	Depression symptoms	HADS	Type D independently predicted persistence of anxiety symptoms, adjusting for depression
van Gestel ³⁶ (2007) <i>J Affect Disord</i>	CAD n=416	Depression symptoms	HADS	Type D independently predicted increased anxiety symptoms, adjusting for depression
Schiffer ³⁷ (2008) <i>J Affect Disord</i>	CHF n=149	Depression symptoms	BDI	Type D independently predicted clinically significant anxiety; depression did not predict anxiety
Wikman ⁶¹ (2008) <i>Psychosom Med</i>	ACS n=213	Depression symptoms	BDI	Type D related to posttraumatic symptoms; after adjustment for depression, no longer significant

ACS indicates acute coronary syndromes; BDI, Beck Depression Inventory; CAD, coronary artery disease; CHF, chronic heart failure; CIDI, Composite International Diagnostic Interview; *EJCPR*, *European Journal of Cardiovascular Prevention and Rehabilitation*; HADS, Hospital Anxiety and Depression Scale; HAM-D, Hamilton Depression rating scale; HPPQ, Heart Patients Psychological Questionnaire; ICD, implantable cardioverter-defibrillator; IHD, ischemic heart disease; MBHI, Millon Behavioral Health Inventory; MQ-D, depression subscale of the Maastricht Questionnaire; and MI, myocardial infarction.

in outcomes research. Research from our group is not limited to Type D but also focuses on anxiety,² depression,⁶⁴ and anhedonia.⁶⁵ Hence, we propose to capitalize on the simultaneous use of specific and general measures of distress in cardiac research and practice. This review provides both empirical and conceptual reasons to further explore Type D as a general propensity to psychological distress that affects cardiovascular outcomes.

Limitations of the Type D Construct

The fact that all prognostic studies included in the quantitative analysis reported on findings from our research group precluded an independent rating of the quality of studies. Hence, replication in other cultures and by other research groups is needed. Recent publications from independent research groups are promising and support the role of Type D as a determinant of genetic,⁶⁶ biological,^{53,54,67–72} and behavioral^{73–79} pathways of disease that promote a better understanding of the effect of psychological distress on cardiac disorder.

There are also mixed findings on Type D personality. In a study of coronary patients, adjustment for depression attenuated the relation between Type D and posttraumatic stress.⁶¹ Recently, we found that neither Type D personality nor anxiety/depression symptoms were related to cardiac mortality in heart failure patients,⁸⁰ but the power of this study was low. Other very recent studies from our group showed that Type D independently predicted an increased risk of mortality after myocardial infarction⁴⁹ or implantable cardioverter-defibrillator treatment (S.S. Pedersen, PhD; unpublished data, 2010) and that Type D accounted for the observed association between suppressed anger and adverse events.⁸¹ Although one study found that depression and not Type D was related to atrial fibrillation,⁵¹ another reported that Type D predicted poor outcome of atrial fibrillation.⁸² In patients with pulmonary disease, depressive symptoms and not Type D predicted mortality,⁸³ whereas other research groups showed that Type D was associated with impaired health status in patients with sleep apnea,⁷⁵ mild brain injury,⁷⁶ Parkinson disease,⁸⁴ gastrointestinal disorders,⁸⁵ or medical comorbidities⁷⁸ and in individuals from the general population.⁸⁶ Our group showed

that Type D was related to poor health status in melanoma survivors.⁸⁷

In the literature, there is an ongoing discussion whether Type D is more accurately represented as a dimensional rather than categorical construct.⁸⁸ Dimensional and categorical approaches to personality are not mutually exclusive but represent 2 ways of capturing psychological tendencies of individuals.⁷⁸ Type D refers to individuals who are more similar to their subgroup's personality profile than other personality profiles,⁶² but, of course, individuals belong only probabilistically to these subgroups. However, similar patterns of standing along the negative affectivity and social inhibition traits do occur across patients, constituting reliable configurations summarized by Type D.⁷⁸

Incremental Value of the Type D Construct

Despite its limitations, the Type D construct has much explanatory and predictive power. The Type D construct was derived from personality theory,²² and recent data support its genetic underpinnings⁶⁶ and heritability.⁸⁹ The Type D classification in cardiac patients is not confounded by temporary changes in mood status¹⁵ or depressive symptoms⁴⁵ and is stable over time.⁴⁵ Neuroimaging research also shows that Type D is related to emotion processing in the brain, as indicated by a decreased differential activity in the amygdale.⁹⁰

Type D personality is characterized by high neuroticism, low extraversion, and low conscientiousness, but these traits and Type D share less than 50% variance¹⁵ and thus are not interchangeable. Head-to-head comparisons of neuroticism, extraversion, and Type D indicated that Type D had unique empirical value in patients with brain injury⁷⁶ or medical comorbidities⁷⁸ and that Type D independently predicted posttraumatic stress⁹¹ and adverse events⁹² in cardiac patients. Type D is also related to increased stress reactivity⁶⁸ and poor health behavior,⁷³ adjusting for hostility or neuroticism. Type D is distinct from repressive coping, with both traits independently predicting cardiac events.⁹³ Hence, authors from other groups have noted that Type D is a new personality construct that contributes to our understanding of the cardiovascular effects of stress⁶⁸ and that Type D “embodies unique information relevant to health that is not captured by multiple trait ratings.”⁷⁸

Biological and Behavioral Pathways

Although the diagnosis of cardiac disease may perhaps affect self-ratings of personality,¹³ it is less likely that Type D is a response to disease. Unlike the association between left ventricular dysfunction and depression,⁵⁰ Type D is not confounded by severity of cardiac disorder^{45,50} or heart failure.⁹⁴ The Type D scale does not include somatic symptoms, and Type D predicts adverse events, adjusting for disease severity and other clinical risk factors.

There are plausible pathways that may explain the increase in risk in Type D patients. In experimental research, Type D has been related to higher cardiovascular stress reactivity, including increased heart rate, blood pressure and cardiac output,^{67,68} and decreased heart rate variability.⁶⁹ In cardiac patients, Type D personality has been associated with reduced heart rate recovery⁷⁰ and with the incidence of ventricular arrhythmia.⁵² A dysfunctional hypothalamic-pituitary-adrenal axis comprises another potential pathway.⁷¹ Type D is related to greater cortisol reactivity to stress⁶⁸ and to increased awakening⁵³ and daytime⁵⁴ cortisol levels in coronary patients. In heart failure patients, Type D personality is associated with increased activity of proinflammatory cytokines⁹⁵ and a dysfunctional cytokine network.⁹⁶ Other heart failure studies found that Type D was independently associated with increased oxidative stress⁵⁵ and that bone marrow-derived progenitor cells numbers were reduced by more than 50% in Type D as compared with non-Type D patients.⁹⁷

Behavioral mechanisms include an unhealthy lifestyle,⁷³ low adherence to medical treatment,^{74,75} and reluctance to consult clinical staff.⁹⁸ In general, Type D individuals are less likely to get a regular medical checkup.⁷³ The inhibited interpersonal style of Type D patients may impede effective communication with their attending physician. Heart failure patients with a Type D personality experience more cardiac symptoms than non-Type Ds but, paradoxically, may be less likely to consult for these symptoms.⁹⁸ Type D also predicts poor medication adherence after myocardial infarction,⁷⁴ and Type D individuals are less likely to adhere to continuous positive airway pressure treatment of obstructive sleep apnea.⁷⁵ Finally, Type D individuals are vulnerable to stress²⁴ and have a limited ability to bounce back from stressful events.⁷⁷ In the face of stress, they use more passive coping strategies (eg, disengagement)⁷⁹ and are not likely to seek appropriate mental care.⁷³

Toward More Individualized Cardiac Care

The relationship between mind and heart is complex.⁹⁹ Because health care providers are trained to “find patterns” and think categorically,⁷⁸ the delineation of Type D may help them to identify high-risk patients.⁶² A broader conceptualization of psychological distress as a cardiovascular risk marker has often wrongly been considered as being too vague.⁶ Broad immunomodulation therapy that focuses on cytokine networks is more successful in improving cardiac survival as compared with therapies that target specific, single cytokines.¹⁰⁰ In analogy, it is possible that a broad approach to behavioral intervention that targets the network of emotional and social problems might also enhance survival in cardiac patients¹⁰¹ and that Type D patients in particular

may benefit from such an approach. Cardiac patients are not “doomed” because they have a Type D personality; in fact, Type D patients may learn new strategies to reduce their level of distress and to improve their social skills.¹⁰² Type D personality has now been included in 2 ongoing randomized, controlled behavioral intervention trials in Italian¹⁰³ and German¹⁰⁴ cardiac patients, and new studies from our own group will also examine whether the risk associated with Type D can be modified.

Psychological distress as a prognostic risk marker does not fall into the “one size fits all” category but includes many different facets.⁹⁹ The summary of findings in this article suggests that Type D may be such a factor. People differ substantially in their level of vulnerability to psychological distress and the assessment of Type D may flag patients that have a more than 3-fold increased odds of poor prognosis or other adverse health outcomes. Of course, the reliability of this estimated risk only applies to those specific populations that were included in our studies. Hence, it is not possible to generalize the results of the current quantitative analyses to other cardiovascular populations without further independent studies. One should also keep in mind that Type D research does not assert any causal claim regarding the incidence of cardiovascular disease but is merely focused on the association between general distress and prognosis in cardiovascular populations.

Assessment of Type D personality may also increase our understanding of substantial interpatient variability in the outcome of invasive treatments such as coronary bypass surgery,⁵⁹ coronary stenting,²⁵ implantation of cardioverter-defibrillators,⁵² or heart transplantation²⁹ that cannot be explained by clinical risk factors. Outcomes research focuses on patient-centered health outcomes such as health status,¹⁰⁵ but there is a gap in our understanding of the determinants of these outcomes.¹⁰⁶ Previous research has focused on age¹⁰⁷ and sex¹⁰⁸ differences in cardiovascular outcomes. Findings from Type D research indicate that individual differences in general distress should also be accounted for when quantifying these outcomes.^{31–40,57–60} In addition, Type D has been related to poor health in conditions such as sleep apnea,⁷⁵ brain injury,⁷⁶ or cancer.⁸⁷ Finally, Type D has been associated with an increased risk of suicidal ideation, adjusting for depressive symptoms.¹⁰⁹

This summary article is largely limited to reports from our own group. Type D personality is a new construct, and there is a need for prospective studies from independent researchers. Lately, the number of Type D studies from other research groups has increased rapidly. Although some have reported negative findings,^{51,56,83} most of these studies support the role of Type D personality as a determinant of mechanisms of disease^{53,54,66–79} and impaired health status in clinical^{59,61,75,76,78,82,84,85} and nonclinical^{73,74,77,79,86} populations. This summary indicates that in addition to depression, a general propensity to distress, as defined by standing on negative affectivity and social inhibition in the Type D model, affects cardiovascular outcomes. Type D only partly overlaps with depression and provides additional health-relevant information that is not captured by other trait ratings.⁷⁸ Currently, individual differences in the general

propensity to psychological distress are largely ignored in outcomes research. With the introduction of the 14-item Type D Scale (DS14) as a brief measurement tool,¹⁵ this “individual difference” assessment of general distress can be easily accomplished with little patient burden and may enhance individualized cardiac care.¹¹⁰

Sources of Funding

This study was supported by VICI grant 453-04-004 from The Netherlands Organization for Scientific Research (The Hague, The Netherlands) to Dr Denollet.

Disclosures

None.

References

- Kubzansky LD, Cole SR, Kawachi I, Vokonas P, Sparrow D. Shared and unique contributions of anger, anxiety, and depression to coronary heart disease: a prospective study in the Normative Aging Study. *Ann Behav Med.* 2006;31:21–29.
- Roest AM, Martens EJ, de Jonge P, Denollet J. Anxiety and risk of incident coronary heart disease: a meta-analysis. *J Am Coll Cardiol.* 2010;56:38–46.
- Shen BJ, Avivi YE, Todaro JF, Spiro A III, Laurenceau JP, Ward KD, Niaura R. Anxiety characteristics independently and prospectively predict myocardial infarction in men: the unique contribution of anxiety among psychologic factors. *J Am Coll Cardiol.* 2008;51:113–119.
- Frasure-Smith N, Lespérance F. Depression and anxiety as predictors of 2-year cardiac events in patients with stable coronary artery disease. *Arch Gen Psychiatry.* 2008;65:62–71.
- Ladwig KH, Baumert J, Marten-Mittag B, Kolb C, Zrenner B, Schmitt C. Posttraumatic stress symptoms and predicted mortality in patients with implantable cardioverter-defibrillators: results from the prospective living with an implanted cardioverter-defibrillator study. *Arch Gen Psychiatry.* 2008;65:1324–1330.
- Gallo L, Matthews KA. Understanding the association between socioeconomic status and physical health: do negative emotions play a role? *Psychol Bull.* 2003;129:10–51.
- Bleil ME, Gianaros PJ, Jennings JR, Flory JD, Manuck SB. Trait negative affect: toward an integrated model of understanding psychological risk for impairment in cardiac autonomic function. *Psychosom Med.* 2008;70:328–337.
- Denollet J. Biobehavioral research on coronary heart disease: where is the person? *J Behav Med.* 1993;16:115–141.
- Barefoot JC, Schroll M. Symptoms of depression, acute myocardial infarction, and total mortality in a community sample. *Circulation.* 1996;93:1976–1980.
- Ruberman W, Weinblatt E, Goldberg JD, Chaudhary BS. Psychosocial influences on mortality after myocardial infarction. *N Engl J Med.* 1984;311:552–559.
- Horsten M, Mittleman MA, Wamala SP, Schenck-Gustafsson K, Orth-Gomér K. Depressive symptoms and lack of social integration in relation to prognosis of CHD in middle-aged women: the Stockholm Female Coronary Risk Study. *Eur Heart J.* 2000;21:1072–1080.
- Razzini C, Bianchi F, Leo R, Fortuna E, Siracusano A, Romeo F. Correlations between personality factors and coronary artery disease: from Type A behaviour pattern to Type D personality. *J Cardiovasc Med.* 2008;9:761–768.
- Stepoe A, Molloy GJ. Personality and heart disease. *Heart.* 2007;93:783–784.
- Denollet J, Sys SU, Brutsaert DL. Personality and mortality after myocardial infarction. *Psychosom Med.* 1995;57:582–591.
- Denollet J. DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. *Psychosom Med.* 2005;67:89–97.
- Pedersen SS, Denollet J. Is Type D personality here to stay? Emerging evidence across cardiovascular disease patient groups. *Curr Cardiol Rev.* 2006;2:205–213.
- Kupper N, Denollet J. Type D personality as a prognostic factor in heart disease: assessment and mediating mechanisms. *J Pers Assess.* 2007;89:265–276.
- Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. *Ann Intern Med.* 2007;147:573–577.
- Vandenbroucke JP, Von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *Ann Intern Med.* 2007;147:W163–W194.
- Lipsey MW, Wilson DB. *Practical Meta-Analysis: Applied Social Research Methods Series.* Vol 49. Thousand Oaks, Calif: Sage Publications; 2001.
- Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Br Med J.* 2003;327:557–560.
- Denollet J, Sys SU, Stoobant N, Rombouts H, Gillebert TC, Brutsaert DL. Personality as independent predictor of long-term mortality in patients with coronary heart disease. *Lancet.* 1996;347:417–421.
- Denollet J, Vaes J, Brutsaert DL. Inadequate response to treatment in coronary heart disease: adverse effects of Type D personality and younger age on 5-year prognosis and quality of life. *Circulation.* 2000;102:630–635.
- Denollet J, Pedersen SS, Vrints CJ, Conraads VM. Usefulness of Type D personality in predicting five-year cardiac events above and beyond current symptoms of stress in patients with coronary heart disease. *Am J Cardiol.* 2006;97:970–973.
- Pedersen SS, Lemos PA, van Vooren PR, Liu TK, Daemen J, Erdman RA, Smits PC, Serruys PW, van Domburg RT. 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 substudy. *J Am Coll Cardiol.* 2004;44:997–1001.
- Pedersen SS, Denollet J, Ong ATL, Sonnenschein K, Erdman RAM, Serruys PW, Van Domburg RT. Adverse clinical events in patients treated with sirolimus-eluting stents: the impact of Type D personality. *Eur J Cardiovasc Prev Rehabil.* 2007;14:135–140.
- Denollet J, Brutsaert DL. Personality, disease severity, and the risk of long-term cardiac events in patients with a decreased ejection fraction after myocardial infarction. *Circulation.* 1998;97:167–173.
- Schiffer AA, Smith ORF, Pedersen SS, Widdershoven JW, Denollet J. Type D personality and cardiac mortality in patients with chronic heart failure. *Int J Cardiol.* 2010;142:230–235.
- Denollet J, Holmes RVF, Vrints CJ, Conraads VM. Unfavorable outcome of heart transplantation in recipients with Type D personality. *J Heart Lung Transplant.* 2007;26:152–158.
- Aquarius AE, Smolderen KG, Hamming JF, De Vries J, Vriens PW, Denollet J. Type D personality predicts mortality in peripheral arterial disease: a pilot study. *Arch Surg.* 2009;144:728–733.
- Pedersen SS, Middel B. Increased vital exhaustion among Type D patients with ischemic heart disease. *J Psychosom Res.* 2001;51:443–449.
- Pedersen SS, Daemen J, Van de Sande M, Sonnenschein K, Serruys PW, Erdman RAM, Van Domburg RT. Type D personality exerts a stable, adverse effect on vital exhaustion in PCI patients treated with paclitaxel-eluting stents. *J Psychosom Res.* 2007;62:447–453.
- Pedersen SS, Ong ATL, Sonnenschein K, Serruys PW, Erdman RAM, Van Domburg RT. Type D personality and diabetes predict the onset of depressive symptoms in patients after percutaneous coronary intervention. *Am Heart J.* 2006;151:367.e1–367.e6.
- Pedersen SS, Denollet J, Ong ATL, Serruys PW, Erdman RAM, Van Domburg RT. Impaired health status in Type D patients following PCI in the drug-eluting stent era. *Int J Cardiol.* 2007;114:358–365.
- Spindler H, Pedersen SS, Serruys PW, Erdman RAM, Van Domburg RT. Type D personality predicts chronic anxiety following percutaneous coronary intervention in the drug-eluting stent era. *J Affect Disord.* 2007;99:173–179.
- Van Gestel YRBM, Pedersen SS, Van de Sande M, De Jaegere PPT, Serruys PW, Erdman RAM, Van Domburg RT. Type D personality and depressive symptoms predict anxiety 12 months post-percutaneous coronary intervention. *J Affect Disord.* 2007;103:197–203.
- Schiffer AA, Pedersen SS, Broers H, Widdershoven JW, Denollet J. Type D personality but not depression predicts severity of anxiety in heart failure patients at 1-year follow-up. *J Affect Disord.* 2008;106:73–81.
- Schiffer AA, Pedersen SS, Widdershoven JW, Denollet J. Type D personality and depressive symptoms are independent predictors of impaired health status in chronic heart failure. *Eur J Heart Fail.* 2008;10:802–810.

39. Aquarius AE, Denollet J, De Vries J, Hamming JF. Poor health-related quality of life in patients with peripheral arterial disease: Type D personality and severity of peripheral arterial disease as independent predictors. *J Vasc Surg*. 2007;46:505–512.
40. Aquarius AE, Denollet J, Hamming JF, Van Berge Henegouwen DP, De Vries J. Type D personality and ankle brachial index as predictors of impaired quality of life and depressive symptoms in peripheral arterial disease. *Arch Surg*. 2007;142:662–667.
41. Denollet J, Pedersen SS, Ong ATL, Erdman RAM, Serruys PW, van Domburg RT. Social inhibition modulates the effect of negative emotions on cardiac prognosis following percutaneous coronary intervention in the drug-eluting stent era. *Eur Heart J*. 2006;27:171–177.
42. Denollet J, Pedersen SS. Prognostic value of Type D personality compared with depressive symptoms. *Arch Intern Med*. 2008;168:431–432.
43. Denollet J, de Jonge P, Kuyper A, Schene AH, van Melle JP, Ormel J, Honig A. Depression and Type D personality represent different forms of distress in the Myocardial Infarction and Depression–Intervention Trial (MIND-IT). *Psychol Med*. 2009;39:749–756.
44. Pelle AJ, Denollet J, Zwisler AD, Pedersen SS. Overlap and distinctiveness of psychological risk factors in patients with ischemic heart disease and chronic heart failure: are we there yet? *J Affect Disord*. 2009;113:150–156.
45. Martens EJ, Kupper N, Pedersen SS, Aquarius AE, Denollet J. Type D personality is a stable taxonomy in post-MI patients over an 18-month period. *J Psychosom Res*. 2007;63:545–550.
46. Spindler H, Kruse C, Zwisler A-D, Pedersen SS. Increased anxiety and depression in Danish cardiac patients with a Type D personality: Cross-validation of the Type D Scale (DS14). *Int J Behav Med*. 2009;16:98–107.
47. Smith OR, Pedersen SS, Van Domburg RT, Denollet J. Symptoms of fatigue and depression in ischemic heart disease are driven by personality characteristics rather than disease stage: a comparison of CAD and CHF patients. *Eur J Cardiovasc Prev Rehabil*. 2008;15:583–588.
48. Martens EJ, Smith OR, Winter J, Denollet J, Pedersen SS. Cardiac history, prior depression and personality predict course of depressive symptoms after myocardial infarction. *Psychol Med*. 2008;38:257–264.
49. Martens EJ, Mols F, Burg MM, Denollet J. Type D personality predicts clinical events after myocardial infarction, above and beyond disease severity and depression. *J Clin Psychiatry*. 2010;71:778–783.
50. de Jonge P, Denollet J, van Melle JP, Kuyper A, Honig A, Schene AH, Ormel J. Associations of Type D personality and depression with somatic health in myocardial infarction patients. *J Psychosom Res*. 2007;63:477–482.
51. Lange HW, Herrmann-Lingen C. Depressive symptoms predict recurrence of atrial fibrillation after cardioversion. *J Psychosom Res*. 2007;63:509–513.
52. van den Broek KC, Nyklíček I, van der Voort PH, Alings M, Meijer A, Denollet J. Risk of ventricular arrhythmia following implantable defibrillator treatment in anxious Type D patients. *J Am Coll Cardiol*. 2009;54:531–537.
53. Whitehead DL, Perkins-Porras L, Strike PC, Magid K, Steptoe A. Cortisol awakening response is elevated in acute coronary syndrome patients with Type D personality. *J Psychosom Res*. 2007;62:419–425.
54. Molloy GJ, Perkins-Porras L, Strike PC, Steptoe A. Type D personality and cortisol in survivors of acute coronary syndrome. *Psychosom Med*. 2008;70:863–868.
55. Kupper N, Gidron Y, Winter J, Denollet J. The association between Type D personality, depression and oxidative stress in chronic heart failure patients. *Psychosom Med*. 2009;71:973–980.
56. Bhattacharyya MR, Perkins-Porras L, Whitehead DL, Steptoe A. Psychological and clinical predictors of return to work after acute coronary syndrome. *Eur Heart J*. 2007;28:160–165.
57. Mols F, Martens EJ, Denollet J. Type D personality and depressive symptoms are independent predictors of impaired health status following acute myocardial infarction. *Heart*. 2010;96:30–35.
58. Smith OR, Michielsen HJ, Pelle AJ, Schiffer AA, Winter JB, Denollet J. Symptoms of fatigue in chronic heart failure patients: clinical and psychological predictors. *Eur J Heart Fail*. 2007;9:922–927.
59. Al-Ruzzeh S, Athanasiou T, Mangoush O, Wray J, Modine T, George S, Amrani M. Predictors of poor mid-term health related quality of life after primary isolated coronary artery bypass grafting surgery. *Heart*. 2005;91:1557–1562.
60. Pelle AJ, Erdman RA, van Domburg RT, Spiering M, Kazemier M, Pedersen SS. Type D patients report poorer health status prior to and after cardiac rehabilitation compared to non-Type D patients. *Ann Behav Med*. 2008;36:167–175.
61. Wikman A, Bhattacharyya M, Perkins-Porras L, and Steptoe, A. Persistence of posttraumatic stress symptoms 12 and 36 months after acute coronary syndrome. *Psychosom Med*. 2008;70:764–772.
62. Denollet J. Type D personality: a potential risk factor refined. *J Psychosom Res*. 2000;49:255–266.
63. Kudielka BM, von Känel R, Gander ML, Fischer JE. The interrelationship of psychosocial risk factors for coronary artery disease in a working population: do we measure distinct or overlapping psychological concepts? *Behav Med*. 2004;30:35–43.
64. Denollet J, Martens EJ, Smith OR, Burg MM. Efficient assessment of depressive symptoms and their prognostic value in myocardial infarction patients. *J Affect Disord*. 2010;120:105–111.
65. Denollet J, Pedersen SS, Daemen J, de Jaegere PT, Serruys PW, van Domburg RT. Reduced positive affect (anhedonia) predicts major clinical events following implantation of coronary-artery stents. *J Intern Med*. 2008;263:203–211.
66. Ladwig K-H, Emeny RT, Gieger C, Ruf E, Klopp N, Illig T, Meitinger T, Wichmann H-E. Single nucleotide polymorphisms associations with Type D personality in the general population: findings from the KORA K-500-Substudy [abstract]. *Psychosom Med*. 2009;71:A-28.
67. Williams L, O'Carroll RE, O'Connor RC. Type D personality and cardiac output in response to stress. *Psychol Health*. 2009;24:489–500.
68. Habra ME, Linden W, Anderson JC, Weinberg J. Type D personality is related to cardiovascular and neuroendocrine reactivity to acute stress. *J Psychosom Res*. 2003;55:235–245.
69. Martin LA, Doster JA, Critelli JW, Lambert PL, Purdum M, Powers C, Prazak M. Ethnicity and Type D personality as predictors of heart rate variability. *Int J Psychophysiol*. 2010;76:118–121.
70. von Känel R, Barth J, Kohls S, Saner S, Znoj H, Saner G, Schmid JP. Heart rate recovery after exercise in chronic heart failure: role of vital exhaustion and Type D personality. *J Cardiol*. 2009;53:248–256.
71. Sher L. Type D personality: the heart, stress, and cortisol. *Q J Med*. 2005;98:323–329.
72. Fischer JC, Kudielka BM, von Kanel R, Siegrist J, Thayer JF, Fischer JE. Bone-marrow derived progenitor cells are associated with psychosocial determinants of health after controlling for classical biological and behavioral cardiovascular risk factors. *Brain Behav Immun*. 2009;23:419–426.
73. Williams L, O'Connor RC, Howard S, Hughes BM, Johnston DW, Hay JL, O'Connor DB, Lewis CA, Ferguson E, Sheehy N, Grealay MA, O'Carroll RE. Type D personality mechanisms of effect: the role of health-related behavior and social support. *J Psychosom Res*. 2008;64:63–69.
74. Williams L, O'Connor RC, Grubb N, O'Carroll R. Type D personality predicts poor medication adherence in myocardial infarction patients. *Psychol Health* 2010. In press.
75. Broström A, Strömberg A, Mårtensson J, Ulander M, Harder L, Svandberg E. Association of Type D personality to perceived side effects and adherence in CPAP-treated patients with OSAS. *J Sleep Res*. 2007;16:439–447.
76. Stulemeijer M, Andriessen TM, Brauer JM, Vos PE, Van Der Werf S. Cognitive performance after mild traumatic brain injury: the impact of poor effort on test results and its relation to distress, personality and litigation. *Brain Injury*. 2007;21:309–318.
77. Smith BW, Dalen J, Wiggins K, Tooley E, Christopher P, Bernard J. The brief resilience scale: assessing the ability to bounce back. *Int J Behav Med*. 2008;15:194–200.
78. Chapman BP, Duberstein PR, Lyness JM. The distressed personality type: replicability and general health associations. *Eur J Personality*. 2007;21:911–929.
79. Polman R, Borkoles E, Nicholls AR. Type D personality, stress, and symptoms of burnout: the influence of avoidance coping and social support. *Br J Health Psychol* 2010. [Epub ahead of print; PMID: 19930789].
80. Pelle AJ, Pedersen SS, Schiffer AA, Szabó BM, Widdershoven JW, Denollet J. Psychological distress and mortality in systolic heart failure. *Circ Heart Fail*. 2010;3:261–267.
81. Denollet J, Gidron J, Vrints CJ, Conraads VM. Anger, suppressed anger, and risk of adverse events in patients with coronary artery disease. *Am J Cardiol*. 2010;105:1555–1560.
82. Ahmed S, Ranchor AV, Rienstra M, Wiesfeld AC, Van Veldhuisen DJ, Van Gelder IC. Effect of Type D personality on success of rhythm

- control therapy for atrial fibrillation and quality of life during amiodarone treatment. *Eurpace*. 2009. doi:10.1093/europace/eup171.
83. de Voogd JN, Wempe JB, Postema K, van Sonderen E, Ranchor AV, Coyne JC, Sanderman R. More evidence that depressive symptoms predict mortality in COPD patients: is Type D personality an alternative explanation? *Ann Behav Med*. 2009;38:86–93.
 84. Dubayova T, Nagyova I, Havlikova E, Rosenberger J, Gdovinova Z, Middel B, van Dijk JP, Groothoff JW. The association of Type D personality with quality of life in patients with Parkinson's disease. *Aging Ment Health*. 2009;13:905–912.
 85. Hansel SL, Umar SB, Lunsford TN, Harris LA, Dibaise JK, Crowell MD. Personality traits and impaired health-related quality of life in patients with functional gastrointestinal disorders. *Clin Gastroenterol Hepatol*. 2010;8:220–222.
 86. Hausteiner C, Klupsch D, Emeny R, Baumert J, Ladwig KH; for the KORA Investigators. Clustering of negative affectivity and social inhibition in the community: prevalence of Type D personality as a cardiovascular risk marker. *Psychosom Med*. 2010;72:163–171.
 87. Mols F, Holterhues C, Nijsten T, van de Poll-Franse LV. Personality is associated with health status and impact of cancer among melanoma survivors. *Eur J Cancer*. 2010;46:573–580.
 88. Ferguson E, Williams L, O'Connor RC, Howard S, Hughes BM, Johnston DW, Allan JL, O'Connor DB, Lewis CA, Grealy MA, O'Carroll RE. A taxometric analysis of Type D personality. *Psychosom Med*. 2009;71:981–986.
 89. Kupper N, Denollet J, de Geus EJ, Boomsma DI, Willemsen G. Heritability of Type D personality. *Psychosom Med*. 2007;69:675–681.
 90. de Gelder B, van de Riet WA, Grèzes J, Denollet J. Decreased differential activity in the amygdala in response to fearful expressions in Type D personality. *Clin Neurophysiol*. 2008;38:163–169.
 91. Pedersen SS, Denollet J. Validity of the Type D personality construct in Danish post-MI patients and healthy controls. *J Psychosom Res*. 2004;57:265–272.
 92. Pedersen SS, Denollet J. Type D and Five Factor personality models of cardiac prognosis: is Type D nothing more than old wine in new bottles? [abstract]. *Psychosom Med*. 2008;70:A26.
 93. Denollet J, Martens EJ, Nyklíček I, Conraads VM, de Gelder B. Clinical events in coronary patients who report low distress: adverse effect of repressive coping. *Health Psychol*. 2008;27:302–308.
 94. Pelle AJ, van den Broek KC, Szabó B, Kupper N. The relationship between Type D personality and chronic heart failure is not confounded by disease severity as assessed by BNP. *Int J Cardiol*. 2010. [Epub ahead of print; PMID: 19477027].
 95. Denollet J, Vrints CJ, Conraads VM. Comparing Type D personality and older age as correlates of tumor necrosis factor- α dysregulation in chronic heart failure. *Brain Behav Immun*. 2008;22:736–743.
 96. Denollet J, Schiffer AA, Kwaijtaal M, Hooijkaas H, Hendriks EH, Widdershoven JW, Kupper N. Usefulness of Type D personality and kidney dysfunction as predictors of interpatient variability in immune activation in chronic heart failure. *Am J Cardiol*. 2009;103:399–404.
 97. Van Craenenbroeck EM, Denollet J, Paelinck BP, Beckers P, Possemiers N, Hoymans VY, Vrints CJ, Conraads VM. Circulating CD34+KDR+ endothelial progenitor cells are reduced in chronic heart failure patients as a function of Type D personality. *Clin Sci*. 2009;117:165–172.
 98. Schiffer AA, Denollet J, Widdershoven JW, Hendriks EH, Smith OR. Failure to consult for symptoms of heart failure in patients with a Type D personality. *Heart*. 2007;93:814–818.
 99. Denollet J, Pedersen SS. Anger, depression and anxiety in cardiac patients: the complexity of individual differences in psychological risk. *J Am Coll Cardiol*. 2009;53:947–949.
 100. Torre-Amione G, Anker SD, Bourge RC, Colucci WS, Greenberg BH, Hildebrandt P, Keren A, Motro M, Moyé LA, Otterstad JE, Pratt CM, Ponikowski P, Rouleau JL, Sestier F, Winkelmann BR, Young JB. Advanced Chronic Heart Failure CLinical Assessment of Immune Modulation Therapy Investigators: results of a non-specific immunomodulation therapy in chronic heart failure (ACCLAIM trial): a placebo-controlled randomised trial. *Lancet* 2008;371:228–236.
 101. Denollet J, Brutsaert DL. Reducing emotional distress improves prognosis in coronary heart disease: 9-year mortality in a clinical trial of rehabilitation. *Circulation*. 2001;104:2018–2023.
 102. Tulloch H, Pelletier R. Does personality matter after all? Type D personality and its implications for cardiovascular prevention and rehabilitation. *Curr Issues Card Rehab Prevention*. 2008;16:2–4.
 103. Roncella A, Girometti A, Cianfrocca C, Pasceri V, Pelliccia F, Denollet J, Pedersen SS, Speciale G, Richichi G, Pristipino C. Rationale and trial design of a randomized, controlled study on short-term psychotherapy after acute myocardial infarction: the STEP-IN-AMI trial (Short Term Psychotherapy in Acute Myocardial Infarction). *J Cardiovasc Med*. 2009;10:947–952.
 104. Albus C, Beutel M, Deter H-C, Fritzsche K, Waller C, Joraschky P, Jordan J, Jünger J, Ladwig K-H, Mück-Weymann M, Söllner W, Herrmann-Lingen C, on behalf of the SPIRR-CAD Study Group (2009). Design and rationale of a new German randomized controlled trial: Stepwise Psychotherapy Intervention for Reducing Risk in Coronary Artery Disease (SPIRR-CAD) [abstract]. *Psychosom Med*. 2009;71:A-89.
 105. Spertus JA. Evolving applications for patient-centered health status measures. *Circulation*. 2008;118:2103–2110.
 106. Krumholz HM, Peterson ED, Ayanian JZ, Chin MH, DeBusk RF, Goldman L, Kiefe CI, Powe NR, Rumsfeld JS, Spertus JA, Weintraub WS; National Heart, Lung, and Blood Institute working group. Report of the National Heart, Lung, and Blood Institute working group on outcomes research in cardiovascular disease. *Circulation*. 2005;111:3158–3166.
 107. Arnold SV, Alexander KP, Masoudi FA, Ho PM, Xiao L, Spertus JA. The effect of age on functional and mortality outcomes after acute myocardial infarction. *J Am Geriatr Soc*. 2009;57:209–217.
 108. Vaccarino V, Parsons L, Peterson ED, Rogers WJ, Kiefe CI, Canto J. Sex differences in mortality after acute myocardial infarction: changes from 1994 to 2006. *Arch Intern Med*. 2009;169:1767–1774.
 109. Michal M, Wiltink J, Till Y, Wild PS, Münzel T, Blankenberg S, Beutel ME. Type D personality and depersonalization are associated with suicidal ideation in the German general population aged 35–74: results from the Gutenberg Heart Study. *J Affect Disord* March 3, 2010. [Epub ahead of print].
 110. Albus C, Jordan J, Herrmann-Lingen C. Screening for psychosocial risk factors in patients with coronary heart disease—recommendations for clinical practice. *Eur J Cardiovasc Prev Rehabil*. 2004;11:75–79.

KEY WORDS: Type D personality ■ depression ■ prognosis ■ health status ■ meta-analysis