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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 disease[1] 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 reflects 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 personality[12–15] 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 marker[1–5] 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

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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)	*Lancet*	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)	*Circulation*	CAD	319	31% (99)	5 years	Cardiac death and MI	OR=8.9	LVEF Age
Denollet[24] (2006)	*Am J Cardiol*	CAD	337	29% (98)	5 years	MACE	OR=2.9	LVEF, index MI, no CABG at baseline Age, sex, psychological stress
Pedersen[25] (2004)	*J Am Coll Cardiol*	CAD	875	29% (254)	¾ year	Death and MI	OR=5.3	Previous CABG, bare vs drug-eluting stent Age, sex
Pedersen[26] (2007)	*Eur J Cardiovasc Prev Rehabil*	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)	*Circulation*	MI	87	31% (27)	6–10 years	Cardiac death and MI	OR=4.8	LVEF, multivessel disease, poor excercise tolerance, history of previous MI Smoking, depression, anxiety, anger
Schiffer[28] (2010)	*Int J Cardiol*	CHF	232	21% (48)	2.6 years	Cardiac death	OR=2.3	LVEF Age, sex
Denollet[29] (2007)	*J Heart Lung Transplant*	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)	*Arch Surg*	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 stenting[41] 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 scale[49] 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)	*Circulation*	CAD	319	31% (99)	5 years	Depressive affect (GMS, NA+/PA−)	OR=2.6	Sex, smoking, depression, anxiety
Pedersen[31] (2001)	*J Psychosom Res*	CAD	171	29% (49)	6 weeks	Vital exhaustion (MQ ≥14)	OR=4.7	NHYA class, cardiac treatment
								Age, sex, education, marital status, work status
Pedersen[32] (2007)	*J Psychosom Res*	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)	*Am Heart J*	CAD	542	17% (94)	½ year	Depressive symptoms (HADS-D ≥8)	OR=3.0	Multivessel disease, stent type, diabetes
								Age, sex
Pedersen[34] (2007)	*Int J Cardiol*	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)	*J Affect Disorders*	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)	*J Affect Disorders*	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)	*J Affect Disorders*	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)	*Eur J Heart Failure*	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)	*J Vasc Surg*	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)	*Arch Surg*	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.

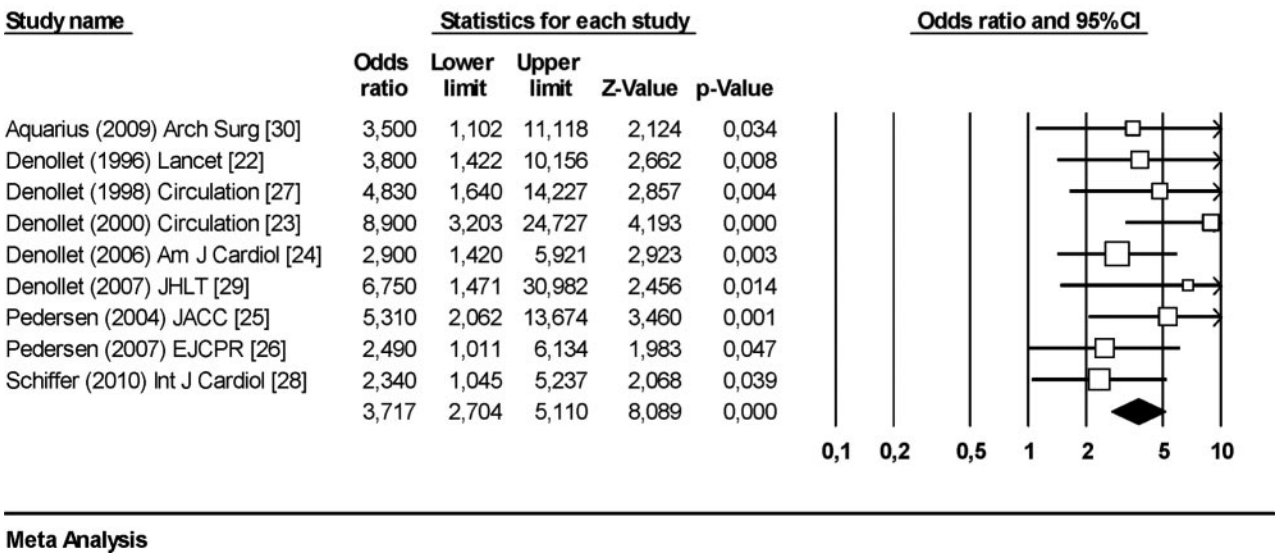

Figure 1. Meta-analysis of Type D personality and prognosis. Note: All odds ratios were multivariably adjusted (see Table 1). EJCPR indicates *Eur J Cardiovasc Prev Rehabil*; JACC, *J Am Coll Cardiol*; and JHLT, *J Heart Lung Transplant.*

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 baseline[33] and predicted the prevalence[46,47] and persistence[48] 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 severity[49] 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.

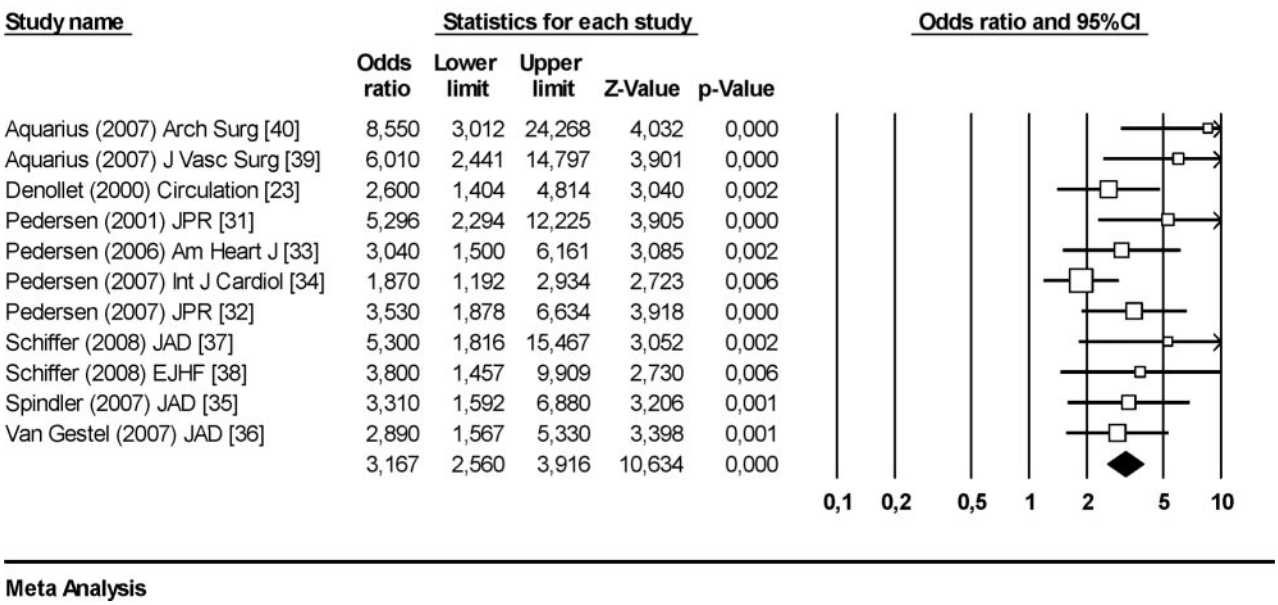

Figure 2. Meta-analysis of Type D personality and emotional distress. Note: All odds ratios were multivariably adjusted (see Table 2). JAD indicates *J Affect Disorders*; and JPR, *J Psychosom Res.*

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 infarction[57] 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 severity[37] 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 mental health,[34,38] and vital exhaustion[32] 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 stress[55] in cardiac patients. Further, Type D predicted the onset,[33] prevalence,[36,46,47] persistence,[35,48] and severity[37] 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) *Psychol Med*	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) *Arch Intern Med*	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) *J Affect Disord*	CAD/CHF n=565	Depression symptoms	BDI HADS	Type D personality traits were distinctly different from depression in factor analysis
Martens[45] (2007) *J Psychosom Res*	MI n=475	Depression symptoms	BDI	Type D classification was not confounded by variability in depressive symptoms over time
Pedersen[33] (2006) *Am Heart J*	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) *Int J Behav Med*	CAD/CHF n=318	Depression symptoms	HADS	Type D independently predicted depression, adjusting for baseline levels of depression
Smith[47] (2008) *EJCPR*	CAD/CHF n=506	Depression symptoms	MQ-D	Type D independently predicted depression, adjusting for baseline levels of depression
Martens[48] (2008) *Psychol Med*	MI n=287	Depression symptoms	BDI	Type D independently predicted persistence of depressive symptoms, adjusting for prior depression
Prognostic differences				
Martens[49] (2010) *J Clin Psychiat*	MI n=473	Depression severity	HAM-D	Type D independently predicted cardiac death/MI, after adjustment for severity of depression
Denollet[42] (2008) *Arch Intern Med*	CAD n=337	Depression symptoms	BDI	Type D independently predicted major adverse cardiac events, adjusting for depression
Denollet[41] (2006) *Eur Heart J*	CAD n=875	Depression symptoms	HADS	Type D independently predicted major adverse cardiac events; depression was not related to events
Denollet[22] (1996) *Lancet*	CAD n=303	Pessimism Despair	MBHI	Type D independently predicted cardiac death; depression only significant in univariate model
Denollet[27] (1998) *Circulation*	MI n=87	Pessimism Despair	MBHI	Type D independently predicted cardiac death/MI; depression only significant in univariate model
Denollet[23] (2000) *Circulation*	CAD n=319	Despondency	HPPQ	Type D independently predicted cardiac death/MI; depression only significant in univariate model
Biological differences				
de Jonge[50] (2007) *J Psychosom Res*	MI n=1205	Affective disorder	CIDI	Type D was not associated with disease severity; depression associated with ventricular dysfunction
Lange[51] (2007) *J Psychosom Res*	AF n=54	Depression symptoms	HADS	Type D was not associated with atrial fibrillation; depression independently predicted atrial fibrillation
van den Broek[52] (2009) *J Am Coll Card*	ICD n=391	Depression symptoms	BDI	Anxious Type D patients were at risk of ventricular arrhythmias; depression not related to arrhythmia
Whitehead[53] (2007) *J Psychosom Res*	CAD n=72	Depression symptoms	BDI	Type D was associated with an increased cortisol awakening response, adjusting for depression
Molloy[54] (2008) *Psychosom Med*	CAD n=70	Depression symptoms	BDI	Type D independently predicted increased cortisol levels; depression was not related to cortisol
Kupper[55] (2009) *Psychosom Med*	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) *Eur Heart J*	ACS n=126	Depression symptoms	BDI	Type D not related to returning to work; depression independently predicted failure to resume work
Schiffer[38] (2008) *Eur J Heart Fail*	CHF n=166	Depression symptoms	BDI	Type D independently predicted poor health status, adjusting for depression
Mols[57] (2010) *Heart*	MI n=503	Depression symptoms	BDI	Type D was associated with poor health status and unstable angina, adjusting for depression
Smith[58] (2007) *Eur J Heart Fail*	CHF n=136	Depression symptoms	BDI	Type D independently predicted symptoms of general fatigue, adjusting for depression
Al-Ruzzeh[59] (2005) *Heart*	CABG n=437	Depression symptoms	HADS	Type D independently predicted poor health status; depression was not associated with health status
Pelle[60] (2008) *Ann Behav Med*	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) *J Affect Disord*	CAD n=167	Depression symptoms	HADS	Type D independently predicted persistence of anxiety symptoms, adjusting for depression
van Gestel[36] (2007) *J Affect Disord*	CAD n=416	Depression symptoms	HADS	Type D independently predicted increased anxiety symptoms, adjusting for depression
Schiffer[37] (2008) *J Affect Disord*	CHF n=149	Depression symptoms	BDI	Type D independently predicted clinically significant anxiety; depression did not predict anxiety
Wikman[61] (2008) *Psychosom Med*	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 infarction[49] 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 comorbidities[78] 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 underpinnings[66] and heritability.[89] The Type D classification in cardiac patients is not confounded by temporary changes in mood status[15] or depressive symptoms[45] 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% variance[15] 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 injury[76] or medical comorbidities[78] and that Type D independently predicted posttraumatic stress[91] and adverse events[92] in cardiac patients. Type D is also related to increased stress reactivity[68] 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 stress[68] 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 recovery[70] 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 stress[68] and to increased awakening[53] and daytime[54] cortisol levels in coronary patients. In heart failure patients, Type D personality is associated with increased activity of proinflammatory cytokines[95] and a dysfunctional cytokine network.[96] Other heart failure studies found that Type D was independently associated with increased oxidative stress[55] 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 stress[24] 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 patients[101] 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 Italian[103] and German[104] 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 transplantation[29] 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 age[107] and sex[108] 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]

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Disclosures

None.

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