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Type D Personality as a Risk Factor for Adverse Outcome in Patients With Cardiovascular Disease: An Individual Patient-Data Meta-analysis

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ABSTRACT

Objective: Type D personality, a joint tendency toward negative affectivity and social inhibition, has been linked to adverse events in patients with heart disease, although with inconsistent findings. Here, we apply an individual patient-data meta-analysis to data from 19 prospective cohort studies (N = 11,151) to investigate the prediction of adverse outcomes by type D personality in patients with acquired cardiovascular disease.

Method: For each outcome (all-cause mortality, cardiac mortality, myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, major adverse cardiac event, any adverse event), we estimated type D's prognostic influence and the moderation by age, sex, and disease type.

Results: In patients with cardiovascular disease, evidence for a type D effect in terms of the Bayes factor (BF) was strong for major adverse cardiac event (BF = 42.5; odds ratio [OR] = 1.14) and any adverse event (BF = 129.4; OR = 1.15). Evidence for the null hypothesis was found for all-cause mortality (BF = 45.9; OR = 1.03), cardiac mortality (BF = 23.7; OR = 0.99), and myocardial infarction (BF = 16.9; OR = 1.12), suggesting that type D had no effect on these outcomes. This evidence was similar in the subset of patients with coronary artery disease (CAD), but inconclusive for patients with heart failure (HF). Positive effects were found for negative affectivity on cardiac and all-cause mortality, with the latter being more pronounced in male than female patients.

Conclusion: Across 19 prospective cohort studies, type D predicts adverse events in patients with CAD, whereas evidence in patients with HF was inconclusive. In both patients with CAD and HF, we found evidence for a null effect of type D on cardiac and all-cause mortality.

Key words: type D personality, cardiovascular disease, meta-analysis, negative affectivity, cardiac events.

INTRODUCTION

Type D ("distressed") personality is defined as the joint tendency toward negative affectivity (NA) and social inhibition (SI). Individuals with high NA have a tendency to experience negative

BF = Bayes factor, **CABG** = coronary artery bypass grafting, **CAD** = coronary artery disease, **CVD** = cardiovascular disease, **MACE** = major adverse cardiac event, **NA** = negative affectivity, **OR** = odds ratio, **PCI** = percutaneous coronary intervention, **SI** = social inhibition

SDC Supplemental Digital Content

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emotions across time and situations, whereas those with high SI tend to feel inhibited and insecure during social interactions (1). Both type D personality traits are associated with other well-known personality traits. For instance, neuroticism correlates positively with both NA ($r = 0.68$) and SI ($r = 0.43$), whereas extraversion correlates negatively with SI ($r = -0.65$) (1). NA also correlates strongly with trait anxiety ($r = 0.81$) (2), and the trait anxiety scale of the Heart Patients Psychological Questionnaire has been used to measure NA before the existence of dedicated type D personality scales such as the Type D Scale-14 (DS14) (1) and Type D Scale-16 (DS16) (3).

Although SI is associated with introversion, it is also a distinct construct because introversion does not necessarily involve a distressed experience, whereas high SI also implies high emotionality and personal distress (2). Although individuals with SI and introverted individuals may both be reticent during social contact, those with SI are so because they feel tense with others, whereas introverted individuals prefer their own company over being with others. SI expresses how people cope with negative emotions, yet it differs from emotional coping styles such as repression and defensiveness because those involve low distress and unconscious exclusion of negative emotions, whereas SI (as measured by, for instance, the DS14) is characterized by high interpersonal distress and conscious suppression of emotions (2). Indeed, the correlation between SI and defensiveness is very small ($r = -0.06$) (3).

Type D personality has been linked to various medical and psychological outcomes (4–6). The cornerstone of type D research is the prognostic risk this distressed personality type is thought to pose to cardiovascular disease (CVD) patients. Previous research has found that individuals who inhibit emotional states are at increased risk of cardiovascular dysregulation and complications, such as decreased heart rate variability (7), cardiovascular recovery (8), and atherosclerosis (9). Moreover, high SI individuals report that they perceive less social support and are less likely to seek help (10). Individuals with high NA and high SI persistently experience negative emotional states and inhibit the expression of these emotions in social situations, thereby increasing their risk on adverse cardiovascular events for which they are not likely to seek help.

Several meta-analyses have indicated that type D personality is associated with an increased risk of adverse events in patients with coronary artery disease (CAD), whereas this has not been found for other types of CVD (4,5). Some have argued that the effect sizes expressing the prognostic risk posed by type D personality have declined over the years, based on the observation that the earlier studies with smaller sample sizes showed larger effects than more recent and larger studies (11). However, others have stated that the difficulty in replicating some of the earlier studies can be explained in terms of differences across studies in end points and patient characteristics such as age and cardiac diagnosis (12). For instance, a meta-analysis concluded an increased mortality risk of type D patients with CAD, but no increased mortality risk in patients with heart failure (HF) (4). Furthermore, a reanalysis of four earlier published studies indicated that in patients with CAD, type D personality was not predictive of all-cause mortality, but it did show an increased risk on cardiac events, primarily in adult patients younger than 70 years (13).

Estimating a Type D Personality Effect

Two constructs synergistically affect another when the conditional effect of each construct on the outcome increases with higher scores on the other construct. Various scholars have argued that a type D effect involves a synergy between its subcomponents NA and SI (14–16). For instance, Denollet et al. (16) claimed that the interaction of emotional distress and inhibition of one's feelings can be viewed as a form of stress that may create or exacerbate serious health problems" (p. 583). Most earlier studies aimed to capture this synergistic effect by classifying people in a type D group when they score high on *both* the NA and SI total scores (1). Various researchers have criticized this *two-group method*, not only for resulting in less statistical power but also for risking spurious type D effects (17,18). A *four-group method* was commonly applied to solve this issue by also including groups for people with high scores on only one of the two NA or SI traits. However, two recent simulation studies showed that not only the two-group method may produce false-positive type D effects when in reality only NA or SI was driving the effect, but that the four-group method to a lesser extent suffers from a similar bias because of the correlation between NA and SI (19,20). In some of these simulated data, only one personality trait (e.g., only NA) was causally related to an outcome. However, analyzing such data with the two-group and four-group methods often produced statistically significant effects of the type D group compared with the other groups. This implies that methods that estimate the type D effect based on two or four personality groups cannot distinguish a causal effect of type D personality from an effect of only one of the underlying personality traits NA or SI.

In line with earlier recommendations (17,18), these simulation studies concluded that of all commonly used methods, the *continuous method*, which does not analyze personality groups but rather the NA and SI total scores, is least biased in detecting various ways in which NA and SI synergistically relate to an outcome measure. This method models the effect of both continuous variables NA and SI, as well as their quadratic effects and interaction. A quadratic effect for NA or SI would imply that the risk this personality trait poses on adverse events is not constant but increases with higher trait scores. Detecting that *both* NA and SI independently predict an outcome would point to an *additive* type D *effect* because the effect of both NA and SI remains constant across the entire score range of these traits. However, researchers have argued that the type D effect involves a synergy between NA and SI (14–16) and that such synergistic effects can be adequately tested by means of an interaction effect between two continuous variables (18–20). If there is an interaction effect between NA and SI on the outcome, then the effect of these traits is not constant, but the effect of one trait changes across scores on the other trait. If the interaction effect is positive, then the effect of one trait on the outcome increases for higher scores on the other trait. We consider such as interaction to reflect a synergy between NA and SI because higher scores on both traits result in increasingly higher predicted values on the outcome measure. Negative interaction effects would not represent a synergistic effect because then the effect of one personality trait on the outcome decreases with higher scores on the other trait.

Reconsidering the Published Type D Literature

Although earlier simulations have indicated that the two-group and four-group methods may lead researchers to erroneously conclude a type D effect when only NA or SI explains variation in the outcome (19,20), the extent of this problem in the type D literature

is still unclear. A recent systematic review of all published studies in the type D literature included all studies that have estimated a type D effect according to both the two-group and continuous method. It turned out that approximately half of the significant two-group effects were not type D effects according to the continuous method, but effects of NA or SI only (21). This suggests a major inconsistency in the conclusions drawn from these two methods, questioning the validity of the conclusions drawn from earlier published studies using only the two-group method. The conclusions of earlier published meta-analyses are equally affected, as those were invariably based on two-group method effects (4,5).

The continuous method, however, is also often not adequately applied. According to earlier simulation studies (19,20), the continuous method should not only include both the NA and SI main effects and their interaction, but also check whether this interaction is confounded by NA and SI *quadratic* effects (22). Most published studies using a continuous method did not model these quadratic NA and SI effects. To the best of our knowledge, only two earlier published studies have done this (23,24). This suggests that for the remaining literature, it stays unclear whether a significant NA × SI interaction indicates a type D effect, or merely a main or quadratic effect of NA or SI. This highlights the importance of reconsidering the published type D literature.

A first reanalysis of type D's prognostic effect in patients with CAD modeled the type D effect according to both the two-group and continuous approaches (13). Both approaches showed that type D increased the risk on cardiac events in patients with CAD. A follow-up analysis revealed that this effect was only found for patients younger than 70 years and did not apply to older patients. Comparisons between older and younger patients may be threatened by survivorship bias in that the older patients may be more resilient to the potential risk their personality trait represented because they have been able to survive for longer. Furthermore, older patients may experience less environmental (work) pressure and may therefore be less susceptible to stress-related cardiac events (13). On the other hand, the increased isolation of older patients can increase their social stress levels (25). It remains unclear why type D personality does not seem to be a risk factor for cardiac events in older individuals with CAD.

Methodological limitations of this previous reanalysis (13) are that the quadratic NA and SI effects were not included and that only the dichotomous method was used to show that the type D effect was less pronounced at older ages, making it unclear whether age moderated the type D effect or whether it moderated a NA or SI effect only. A second limitation is a possible selection bias because the included data originated from four subsequent cohorts from the same university hospital. Individual patient meta-analysis on data from a diverse set of research groups is essential to achieve a more representative sample of studies.

Here, we present the results of an individual patient meta-analysis focusing on type D's prognostic effect in patients with CVD. Individual patient meta-analysis enables an efficient reanalysis of large collections of studies designed to answer a similar research question (26). This results in high statistical power to detect small effects that are hard to detect in each of the included studies individually. Whereas traditional meta-analyses are only able to estimate moderator effects at the study level, individual patient meta-analyses can test moderator effects at the individual level, resulting in more power to detect moderators of type D's prognostic influence.

Our first aim was to aggregate the data of earlier published prospective cohort studies and test the association between type D personality and the occurrence of adverse events during follow-up in patients with CVD. Another aim is to determine whether this type D effect depends on age, sex, and cardiac diagnosis. Previous research has found that male patients with type D personality show a more elevated heart rate response to social tasks than female patients with type D personality (27). Studies have also shown that type D is more predictive of major adverse cardiac event (MACE) in younger ages than older ages (13), and a meta-analysis concluded an increased mortality risk of type D patients with CAD, but no such risk in patients with HF (4). Although our final conclusions will be based on the continuous method, a secondary aim is to estimate the type D effect according to the two-group, four-group, and continuous methods to illustrate the difference in the results they generate. In line with earlier research, we expect (4) that type D personality is a risk factor for cardiac events but not for all-cause mortality and (5) that the type D effect is more pronounced in younger than in older individuals (13).

METHODS

Inclusion Criteria

We only included prospective cohort studies involving patients who at baseline were diagnosed with CVD, CAD, HF, or ventricular arrhythmia, and in which the type D traits NA and SI were measured using the DS16 (3) or DS14 (1) (or any other validated instrument designed to measure these personality traits), and for whom the occurrence of adverse events was recorded over the study's follow-up time. We excluded case-control, cross-sectional studies, imaging studies, case series, and case reports. When several studies had been published on the same cohort, we included the study with the largest sample size and/or longest follow-up time. Of each included study, we contacted the corresponding author (or other authors in case of nonresponse) and requested the raw data listed hereinafter. Included studies at least had to provide data on type D personality (individual item scores or total scores for NA and SI) and adverse outcomes (at least one of the following: all-cause mortality, cardiac mortality, myocardial infarction [MI], coronary artery bypass grafting [CABG], and percutaneous coronary intervention [PCI]). In addition, we requested data regarding clinical characteristics (type of CVD), demographic characteristics (age, sex), and study characteristics (date of baseline measurement, follow-up duration).

Search Strategy

We conducted a literature search on January 4, 2020, using the electronic databases PubMed, Web of Science, and PsycINFO. We updated this literature search on April 1, 2022. We searched for the terms "type D personality" AND ["cardiovascular disease" OR "coronary artery disease" OR "coronary heart disease" OR "heart failure" OR "ventricular arrhythmia"] AND ["adverse event" OR "myocardial infarction" OR "mortality" OR "cardiac death" OR "cardiac event" OR "MACE"]. Furthermore, we performed hand searches, selecting articles included in earlier systematic reviews and meta-analyses. We limited our search to a period between 1996 and January 2020 because the first publication on type D personality was in 1996. Two authors (P.L. and M.A.) independently performed the screening process. In the first step, titles and abstracts

were screened, and studies were included or excluded based on the established criteria. In the second step, inclusion of studies passing the first round was determined by examining the full text. In case of disagreements between the two reviewers (P.L. and M.A.), a third reviewer (N.K.) was consulted. We have used the QUIPS tool to assess the quality of the prospective cohort studies included in our meta-analysis (28). During the quality assessment, we have not evaluated the statistical analysis and inclusion of confounders because we are responsible for those analysis choices in our individual patient-data meta-analysis. Tables S3 and S4 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) present the results of this quality assessment.

Data Extraction

The participating researchers were requested to share their data in either an Excel or SPSS file. Because the shared data already contained all information required to conduct the individual patient-data meta-analysis, it was not necessary to further extract data from the included articles. If raw DS14 item scores were shared, then we checked the calculation of the NA and SI total scores to prevent errors in calculating the total scores (e.g., reverse coding). For each study, the NA and SI scores were standardized within studies to accommodate for the fact that three of the included studies did not use the DS14 questionnaire but other instruments to measure NA and SI that preceded the DS14. Within-cluster (i.e., within-study) standardization is recommended in multilevel studies when effects of person-level predictors (e.g., personality traits) are of primary interest (29).

Operationalizing Type D Personality

We operationalized type D personality according to the continuous interaction method. The Supplemental Digital Content files, http://links.lww.com/PSYMED/A902, contain the methods and results for analyses based on the two-group and four-group methods. The continuous method models both the continuous NA and SI main effects, as well as their interaction. The method further investigates whether the interaction is confounded by quadratic NA or SI effects (20). The quadratic and interaction effects are calculated by multiplying the mean-centered or standardized NA and SI scores. When no quadratic NA or SI effects are found, the interaction effect in the model without the quadratic effects was used to represent the type D effect.

End Points

As end points, we investigated five observed end points such as all-cause mortality, cardiac mortality, MI, CABG, and PCI, and two composite end points such as MACE and any adverse event. *MACE* was defined as the occurrence of cardiac mortality, MI, CABG, or PCI during follow-up. *Any adverse event* was defined as the occurrence of MACE or all-cause mortality during follow-up. If the effect of a composite end point is only driven by one of the observed end points included in the composite, then a significant composite end point could wrongly raise the impression that the other observed end points are also affected (30). Therefore, we did not limit our analyses to these composite end points but also present the findings for each of the directly observed outcomes. The included studies differed in the number of recorded end points. When computing the MACE and any adverse event end points, only studies that recorded each of the end points included in these composites were included. For instance, if a study only recorded cardiac mortality, then this study could not be used in analyses of the MACE or any adverse events end point because it was unknown whether these patients had an MI or underwent CABG or PCI.

Statistical Analysis

We conducted our primary individual patient-data meta-analysis according to a one-stage approach (31). This approach aggregates the data across the included studies and uses a multilevel approach to allow for variation in the estimated regression coefficients across studies. We used a Bayesian estimation procedure to determine the evidence in favor of both the null and the alternative hypotheses. Bayesian multilevel logistic regression models were fitted using the R-package brms (32). All regression coefficients (intercept + predictor coefficients) were modeled as random parameters to capture the dependency between scores of participants included in the same study. Parameters were estimated using Markov Chain Monte Carlo sampling with three chains and 3000 iterations, including 1000 warm-up iterations. The type D personality effects on each end point were estimated according to each of the two-group, four-group, and continuous approaches. Final conclusions were based on the continuous method because this approach is the least biased according to earlier simulation results (19,20). Age and sex were both included as covariates and as potential moderators of the type D effects on each end point. Moderation models were estimated separately for age, sex, and disease type, each model including the interaction effect between age/sex/disease on the one hand and the personality trait variables on the other hand (NA, SI, NA^2, SI^2, NA × SI).

For all models, effects were expressed in terms of odds ratios (ORs), including 95% Bayesian credible intervals. In line with earlier research (33), we assumed the priors of the regression coefficients to be normally distributed $N(\mu = 0, \sigma = 2)$. As a sensitivity analysis, we also investigated the same prior but with smaller or larger standard deviation (SD; $\sigma = 1$ and $\sigma = 4$). For each method, the evidence for a type D effect in terms of the Bayes factor (BF) was quantified as the evidence ratio of the posterior probability of a hypothesis against its alternative. For example, the evidential value for a type D effect according to the continuous method was determined as the ratio of the posterior probability that the regression coefficient of the NA × SI interaction was larger than 0, against the posterior probability that this coefficient was 0 or smaller. To quantify the evidence in favor of the null hypothesis of no type D effect (regression coefficient of NA × SI interaction = 0), BFs were estimated according to the Savage-Dickey density ratio method (34). BFs can be used to quantify the support of one model compared with another model. In contrast to frequentist statistics, this allows us to quantify evidence in favor of a hypothesis (e.g., evidence in favor of the null hypothesis of no type D effect). BFs were interpreted according to guidelines by Kass and Raftery (35) (BFs 1–3.2 = "anecdotal"; BFs 3.2–10 = "substantial"; BFs 10–100 = "strong"; BFs 100 or larger = "decisive").

As a sensitivity analysis, we also conducted two-step meta-analyses to investigate whether the results of our one-step analysis are robust against the selection of a different meta-analytic approach (36). In the first step, logistic regression analyses were conducted to estimate for each end point the association with type D personality according to the continuous method. In the second step, a fixed-effects meta-analysis (37) was conducted for each end point on the log ORs and standard errors estimated in step 1.

The exponentiated (OR) results of those analyses were visualized in forest plots.

All analyses were conducted using R (38), and the script is available on this project's open science framework page, together with the preregistration of the data collection and analysis plan: https://osf.io/czmhs/.

RESULTS

Our initial literature search resulted in 367 unique studies. The flowchart in Figure 1 shows that after reviewing the titles and abstracts, 330 studies were excluded because they either did not use a prospective cohort design or did not involve patients with CVD. Of the resulting 37 studies, an additional 12 were excluded for similar reasons after examining the full text. We emailed the corresponding authors of the remaining 25 eligible studies. In case of no response, we first sent two reminders before emailing other authors. Researchers of 20 studies responded to our emails, and 18 were willing to participate in this project by sharing their data. The authors of the remaining studies did either not respond or indicate that the data could not be shared because projects involving that data set are still in progress. After updating the literature search during the review process, we included one additional study in our analysis, resulting in 19 included prospective cohort studies.

Table 1 shows the characteristics of these 19 studies, comprising a total of 11,151 patients with CVD who were followed for an average follow-up time of 47.1 months (median = 37 months,

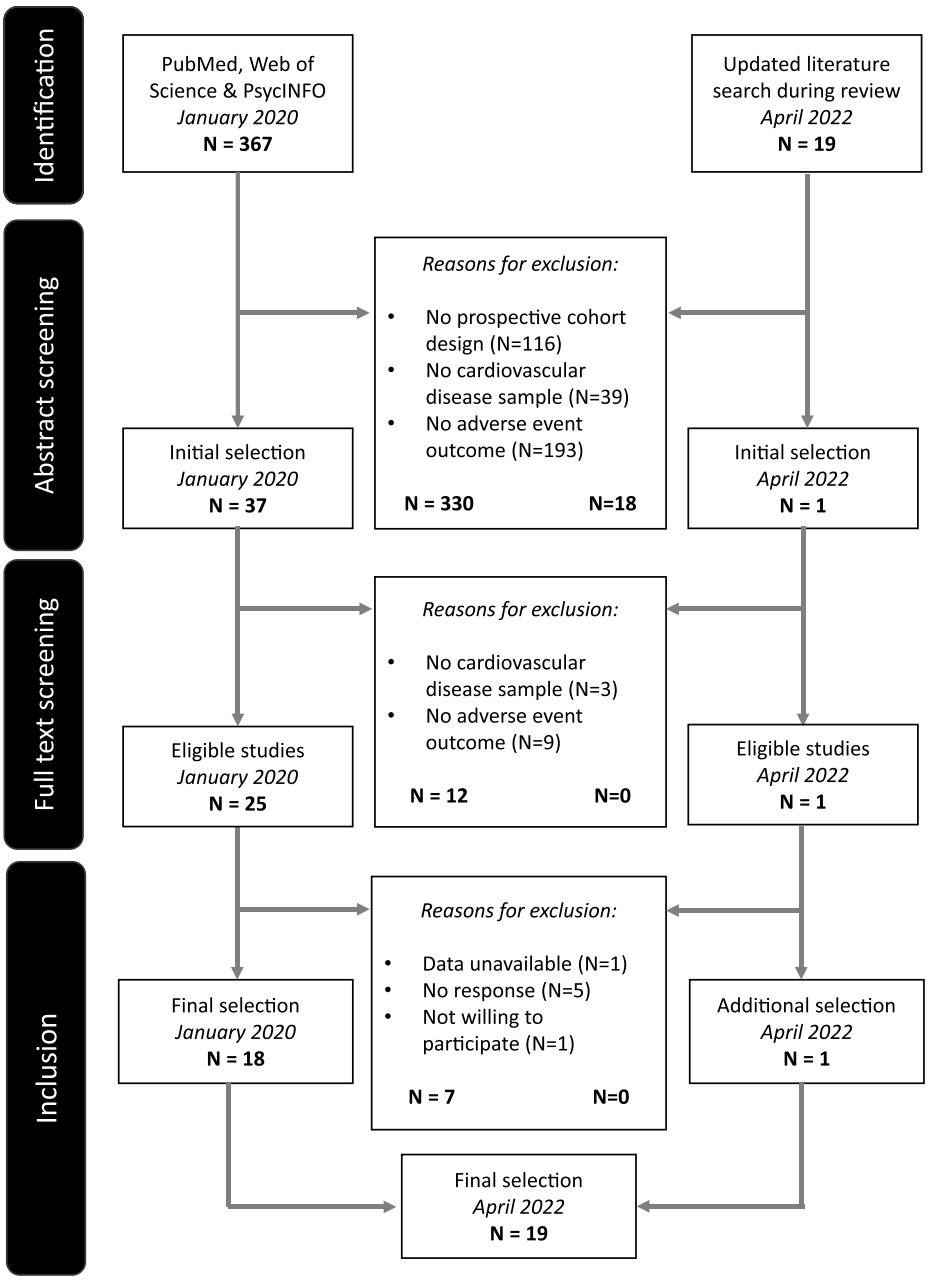

FIGURE 1. Flowchart of the systematic literature review.

TABLE 1. Characteristics of Studies Included in the Individual Patient-Data Meta-analysis

Study	*N*	Diagnosis	Country	Follow-up, mo	Age (M), y	Men, %	Type D Personality Measure	Negative Affectivity, M (SD)	Social Inhibition, M (SD)
Denollet et al. (39)	378	CAD	Belgium	95	55.6	88.6	STAI and HPPQ	9.8 (6.7)	10.5 (6.6)
Denollet et al. (40)	364	CAD	Belgium	60	56.5	91.8	DS16	9.7 (6.6)	14 (6.6)
Denollet et al. (41)	326	CAD	The Netherlands	20	56.8	87.1	DS16	9.2 (6.6)	13.3 (6.3)
Martens et al. (42)	466	CAD	The Netherlands	22	59.3	78.5	DS14	7.3 (6.2)	9.1 (6.5)
Pelle et al. (43)	641	HF	The Netherlands	37	66.4	74.3	DS14	7.1 (6.4)	9.1 (6.5)
Schmidt et al. (44)	137	CAD	Brazil	12	60.2	63.5	DS14	10.6 (6.7)	10.3 (7.4)
Coyne et al. (45)	1047	HF	The Netherlands	18	70.9	62.6	DS14	6.3 (6.0)	7.8 (6.9)
Herrmann-Lingen et al. (46)	569	CAD	Germany	18	59.2	78.9	DS14	15.8 (4.8)	11.8 (5.9)
Grande et al. (47)	1091	MIX	Germany	71	62.7	74.8	DS14	10.1 (5.7)	8.3 (5.2)
Denollet et al. (48)	638	VA	The Netherlands	38	62.9	80.6	DS14	7.5 (6.4)	9.0 (6.3)
Denollet et al. (49)	541	CAD	Belgium	60	58.7	87.4	DS14	9.0 (6.3)	9.8 (6.3)
Meyer et al. (50)	470	CAD	Germany	60	63.7	76.8	DS14	10.6 (5.7)	9.2 (5.7)
Sumin et al. (51)	682	CAD	Russia	12	58.5	81.8	DS14	9.1 (4.1)	9.3 (3.5)
Dulfer et al. (52)	1190	CAD	The Netherlands	120	62.3	72.6	DS14	9.4 (6.8)	9.1 (6.5)
Gostoli et al. (53)	117	VA	Italy	24	63.1	74.4	DS14	8.1 (6.7)	7.4 (6.5)
Pushkarev et al. (54)	939	CAD	Russia	12	58.7	75.3	DS14	10.4 (5.8)	9.7 (5.5)
Conden et al. (55)	941	CAD	Sweden	76	70.5	66.7	DS14	6.6 (5.6)	7.9 (5.8)
Lin et al. (56)	222	HF	Taiwan	18	60.4	66.2	DS14	6.5 (5.1)	6.0 (5.7)
Lv et al. (57)	392	CAD	China	12	61.6	68.9	DS14	11.4 (4.7)	10.9 (4.9)

M (SD) = mean (standard deviation); CAD = coronary artery disease; STAI = State Trait Anxiety Inventory; HPPQ = Heart Patients Psychological Questionnaire; HF = heart failure; MIX = mix of various cardiovascular disease diagnoses; VA = ventricular arrhythmia.

interquartile range = 15.2–63.2 months). The included studies differed in the cardiac diagnosis, age, and sex of patients, but on average (SD), the patients were 62.5 (11.3) years old, most were male (75.6%) and most were diagnosed with CAD (N_{CAD} = 8096; N_{HF} = 2027; N_{VA} = 638; N_{CVD} = 390). Figure 2 visualizes the bivariate distribution of the NA and SI scores in each study. Across all studies, NA and SI were positively correlated (r = 0.373). Tables S3 and S4 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) report the quality assessment of each included study. Although some studies were potentially more biased than others, most were at low risk of bias and none of the included studies showed a high risk of bias.

A Bayesian multilevel logistic regression analysis was used to estimate the type D effects. The number of iterations of the Markov Chain Monte Carlo procedure was sufficient to reach an effective sample size of at least 500 in the estimation of each model parameter. The R-hat value of each estimated regression coefficient was smaller than 1.05, indicating proper convergence (58). Table 2 shows for each end point the estimated ORs (including 95% Bayesian credible interval) of age, sex, the type D effects according to the three operationalizations. Older age and male sex predicted the occurrence of all-cause mortality and cardiac mortality, but none of the other end points. Based on the continuous method, NA and SI showed a synergistic type D effect on the occurrence of any adverse event during follow-up (OR = 1.135, 95% confidence interval [CI] = 1.029–1.253). Although the interaction model including quadratic effects also showed a synergistic type D effect on MACE, when excluding the nonsignificant quadratic NA and SI effects from the continuous interaction model, the 95% Bayesian credible interval contained an OR of 1, suggesting no effect (OR = 1.126, 95% CI = 0.99–1.286). For all other end points, the 95% credible interval of the interaction effect between NA and SI included an OR of 1, suggesting that type D did not predict the occurrence of all-cause mortality, cardiac mortality, MI, CABG, or PCI. However, an NA main effect was found for both all-cause mortality (OR = 1.156, 95% CI = 1.045–1.296) and cardiac mortality (OR = 1.284, 95% CI = 1.088–1.51). Tables S1 and S2 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) show for each end point the SD (including 95% Bayesian credible interval) of all random predictor effects according to the continuous method. The fact that many of these credible intervals did not include an SD of zero suggests that these effects differ across studies, supporting our choice to model these parameters as random effects.

Table 3 presents the BF estimates according to the continuous method, expressing the evidential value for the presence or absence of a type D effect on each end point for the complete sample and for patients with CAD and HF separately. Evidence for a type D effect in the complete sample was strong for the end point MACE (BF = 40.1) and decisive for any adverse event (BF = 99.0). Strong evidence for a null effect was found for all-cause mortality (BF = 47.18), cardiac mortality (BF = 23.34), and MI (BF = 19.29). The evidence for a type D effect on CABG and PCI was inconclusive, showing substantial evidential value both in favor and against a type D effect. When limiting the sample to patients with CAD, similar evidential values were found. For patients with HF, however, substantial to strong evidence was found against a type

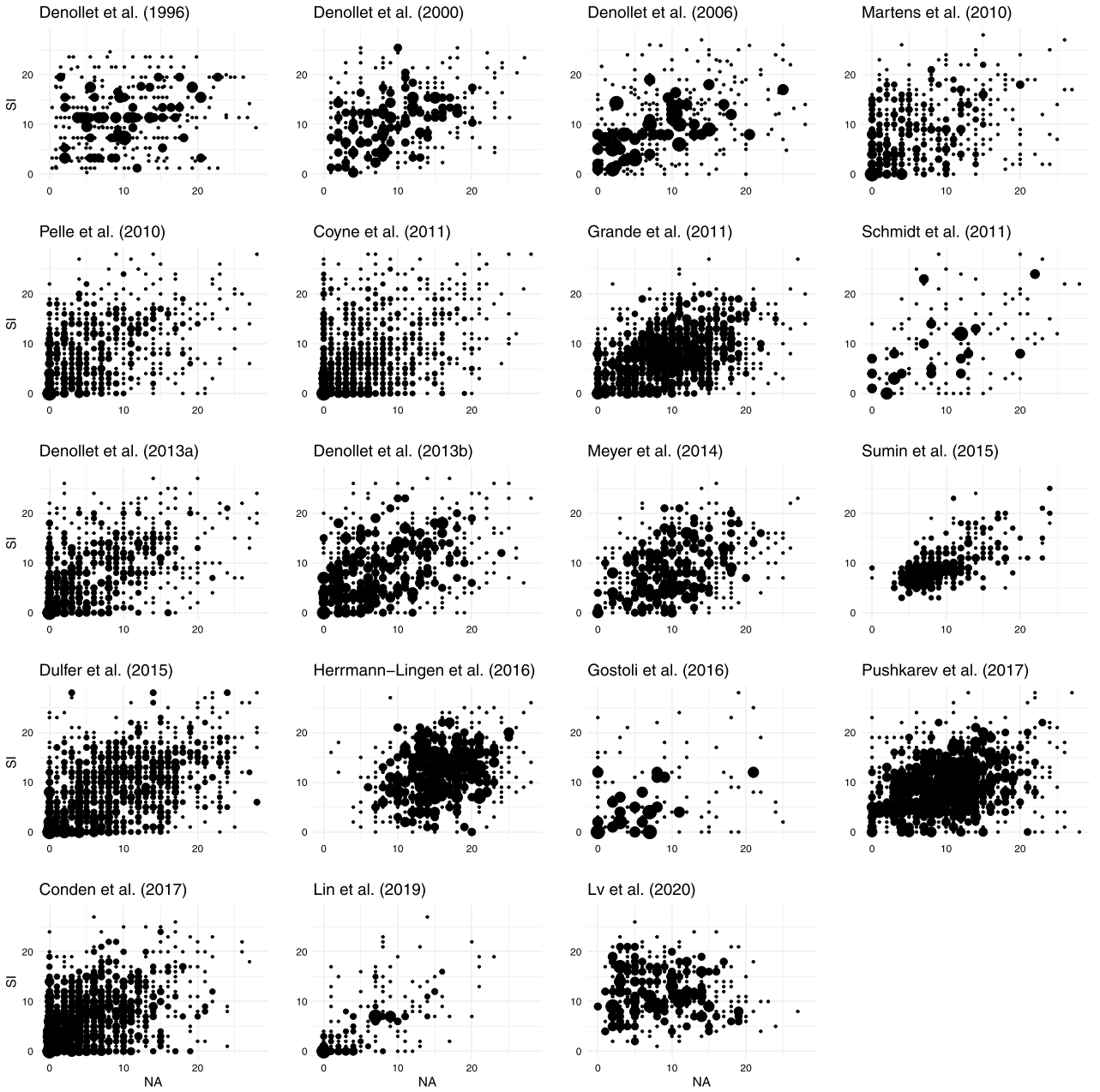

FIGURE 2. For each included study, a scatterplot of the NA and SI sum scores. The dot size represents the frequency of a NA and SI score combination. NA = negative affectivity; SI = social inhibition.

D effect on all-cause mortality (BF = 10.14), whereas for the other end points, the evidence either was inconclusive or could not be estimated because of sparse data.

The results in Table 4 indicate that age, sex, and type of CVD did not moderate the synergistic type D effects (interaction between NA and SI) on any of the studied end points. However, sex turned out to moderate the quadratic NA effect on all-cause mortality, indicating that increasingly higher NA scores were associated with higher odds on all-cause mortality, and this effect was more pronounced for male than for female patients (OR = 1.184, 95% CI = 1.026–1.353). A BF of 89.9 indicated very strong evidence that the population OR of this effect is larger than 1.

Figure 3 visualizes the type D effects on each end point according to the continuous method estimates for the model including the NA and SI main effects and their interaction. For various standardized NA and SI scores, the figure shows the predicted posterior probability on the occurrence of each end point. The colored shades represent the 95% prediction intervals for each level of SI scores. The figure indicates the positive interaction effect between NA and SI on both MACE and any adverse events. The probability on the occurrence of these events during follow-up increased for higher NA scores, and these positive effects became more pronounced for larger scores on SI. Similarly shaped curves but smaller effects were found for CABG or PCI, although statistical evidence

TABLE 2. For Each End Point, the Estimated Odds Ratios (95% Bayesian Credible Interval) of Demographic Predictors, the Type D Effects According to the Continuous Method

Outcome	All-Cause Mortality	Cardiac Mortality	Myocardial Infarction	CABG	PCI	MACE	Any Adverse Event
Sample Size	*n* = 10,647	*n* = 6166	*n* = 6269	*n* = 2832	*n* = 2840	*n* = 4315	*n* = 6013
Predictor	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographics[m3]							
Age (standardized)	**1.933 (1.559 to 2.355)**	**1.56 (1.238 to 1.991)**	1.107 (0.785 to 1.615)	0.945 (0.561 to 1.65)	0.835 (0.674 to 1.032)	1.087 (0.833 to 1.436)	1.14 (0.918 to 1.456)
Men	**1.27 (1.012 to 1.597)**	**1.681 (1.096 to 2.648)**	1.089 (0.735 to 1.676)	0.832 (0.299 to 2.224)	0.725 (0.406 to 1.212)	1.069 (0.762 to 1.461)	1.021 (0.748 to 1.369)
Continuous method							
$NA^{[m1]}$	**1.156 (1.045 to 1.296)**	**1.284 (1.088 to 1.51)**	1.118 (0.96 to 1.325)	1.296 (0.829 to 1.861)	**1.205 (1.002 to 1.435)**	**1.283 (1.146 to 1.44)**	**1.269 (1.139 to 1.425)**
$SI^{[m1]}$	1.011 (0.922 to 1.136)	1.061 (0.873 to 1.341)	1.09 (0.947 to 1.277)	0.977 (0.69 to 1.384)	1.045 (0.874 to 1.247)	1.049 (0.945 to 1.166)	1.05 (0.952 to 1.165)
$NA^{2[m2]}$	1.038 (0.975 to 1.107)	1.054 (0.918 to 1.179)	1.074 (0.977 to 1.181)	1.026 (0.757 to 1.298)	1.004 (0.842 to 1.144)	1.023 (0.948 to 1.101)	1.019 (0.952 to 1.09)
$SI^{2[m2]}$	1.005 (0.916 to 1.084)	0.927 (0.809 to 1.059)	1.076 (0.946 to 1.26)	1.088 (0.82 to 1.422)	1.041 (0.9 to 1.194)	1.058 (0.967 to 1.157)	1.041 (0.962 to 1.126)
$NA \times SI^{[m3]}$	0.996 (0.918 to 1.092)	0.996 (0.851 to 1.191)	1.069 (0.937 to 1.232)	1.171 (0.844 to 1.666)	1.112 (0.896 to 1.351)	**1.14 (1.001 to 1.286)**	**1.167 (1.033 to 1.313)**
$NA \times SI^{[m4]}$	1.02 (0.953 to 1.116)	0.994 (0.870 to 1.142)	1.120 (0.995 to 1.282)	1.165 (0.891 to 1.507)	1.099 (0.884 to 1.308)	1.126 (0.99 to 1.268)	**1.135 (1.029 to 1.253)**

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; MACE = major adverse cardiac event; OR = odds ratio; CI = confidence interval; NA = negative affectivity; SI = social inhibition.

The 95% CI of bold cells does not include an odds ratio of 1.

[m1]: Model = Age + Men + NA + SI.

[m2]: Model = Age + Men + NA + SI + NA^2 + SI^2.

[m3]: Model = Age + Men + NA + SI + NA^2 + SI^2 + NA × SI.

[m4]: Model = Age + Men + NA + SI + NA × SI.

TABLE 3. For Each end point, BF Estimates and Evidential Value for the Presence (Main Hypothesis) or Absence (Null Hypothesis) of a Type D Effect According to the Continuous Methods

	All-Cause Mortality		Cardiac Mortality		Myocardial Infarction		CABG		PCI		MACE		Any Adverse Event	
Type D Effect	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence
Complete sample (N = 11,151)														
Main hypothesis: NA × SI > 0	0.82	Anecdotal	0.86	Anecdotal	5.45	Substantial	4.87	Substantial	6.37	Substantial	**40.1**	**Strong**	**99.0**	**Decisive**
Null hypothesis: NA × SI = 0	**47.18**	**Strong**	**23.34**	**Strong**	**19.29**	**Strong**	8.05	Substantial	9.87	Substantial	3.83	Substantial	1.57	Anecdotal
Patients with CAD (n = 8096)														
Main hypothesis: NA × SI > 0	4.96	Anecdotal	4.04	Anecdotal	3.89	Substantial	5.24	Substantial	6.65	Substantial	**39.0**	**Strong**	**175.47**	**Decisive**
Null hypothesis: NA × SI = 0	**17.38**	**Strong**	**10.98**	**Strong**	**22.35**	**Strong**	8.19	Substantial	9.57	Substantial	3.54	Substantial	1.04	Anecdotal
Patients with HF (n = 2027)[a]														
Main hypothesis: NA × SI > 0	0.55	Anecdotal	0.81	Anecdotal	—	—	—	1.15	Anecdotal	1.24	Anecdotal			
Null hypothesis: NA × SI = 0	**10.14**	**Strong**	4.90	Substantial	—	—	—	2.52	Anecdotal	2.88	Anecdotal			

BF = Bayes factor; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; MACE = major adverse cardiac event; NA = negative affectivity; SI = social inhibition; CAD = coronary artery disease; HF = heart failure.
Bold faced cells indicate strong or decisive evidential value.
[a] Empty cells indicate that insufficient data were available to estimate the type D effect on a particular end point for this patient sample.

for these type D effects was inconclusive. To facilitate the interpretation of these figures, across the included data sets, patients, on averaged (SD), scored 9.02 on the NA (6.33) and 9.20 (6.01) on the SI measurements of the DS14. Based on these statistics, Figure 3 indicates that the probability on any adverse event during follow-up is 0.14 for patients with average NA and SI scores. For patients scoring two SDs above the average on NA (21.7), this risk increases to 0.20. For type D patients, such as those who score two SDs above the average on both NA (21.7) and SI (21.3), the risk of an adverse event increases even further to 0.30. To facilitate the significant interaction effects between NA and SI on any adverse events in patients with CVD, Table S8 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) reports for both NA and SI the simple slope analysis. The effect of SI on adverse events increases across higher NA scores, and the 95% CI of the simple slopes starts to exclude a slope of zero (no effect) at NA scores of 13.8 or higher. The effect of NA on adverse events increases across higher SI scores, and the 95% CI of the simple slope starts to exclude a slope of zero at SI scores of 6.2 or higher.

To facilitate the interpretation of our model estimates, we have created an online tool (https://anonymousresearcher.shinyapps.io/AdverseEvent_Prediction_TypeD_CVD/) that uses the age, sex, NA and SI scores, and type of CVD to calculate, according to our model estimates, the predicted probability on a particular outcome within the average follow-up time of our meta-analysis. For instance, for a 60-year-old male patient with CVD with a high NA score (29), the probability of having an adverse event within 48 months is 40.72% when the SI score is average (1), whereas the probability increases with 4% to 44.85% when the SI score is high (29).

As a sensitivity analysis, Figures S1 to S7 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) show for each end point a forest plot presenting the results of the two-step meta-analyses. These results are like those of the one-step meta-analysis, suggesting that type D personality (operationalized according to the continuous method) was significantly associated with MACE and any adverse event, but not with any of the other end points. Table S5 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) presents the results of leave-one-out sensitivity analyses, which repeat the meta-analysis multiple times, each time with a different study left out. This sensitivity analysis shows that our findings were generally not driven by a single study, except that excluding one of the studies (49) attenuated the type D effect on MACE, resulting in a Bayesian 95% credible interval that included the value of no effect (OR = 1) and suggesting that the MACE effect is largely driven by that study. Another sensitivity analysis reported in Table S6 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) estimated the impact of prior distribution specification for the regression coefficients of the type D effect according to the continuous method. The results show similar conclusions for each end point except MACE, with different prior distributions resulting in similarly sized type D effects, yet slightly wider 95% credible intervals including an OR of no effect, suggesting uncertainty regarding type D's effect on MACE. Lastly, Table S7 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) presents for each method to estimate the type D effect a brier score, expressing the accuracy of predicting the observed end point based on the model estimates. For each method

TABLE 4. For Each End Point, the Estimated Odds Ratios (95% Bayesian Credibility Interval) of the Moderating Influence of Age, Sex, and Disease on the Type D Effects According to the Continuous Method

Outcome	All-Cause Mortality	Cardiac Mortality	Myocardial Infarction	CABG	PCI	MACE	Any Adverse Event
Predictor	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Moderating effect of sex[m1]							
Men × NA	1.05 (0.861–1.269)	0.943 (0.571–1.518)	0.969 (0.696–1.338)	1.301 (0.502–3.174)	0.968 (0.622–1.466)	1.008 (0.755–1.344)	0.964 (0.727–1.257)
Men × SI	0.948 (0.78–1.155)	1.025 (0.66–1.613)	1.006 (0.727–1.395)	0.755 (0.298–1.87)	1.165 (0.782–1.753)	1.088 (0.839–1.427)	1.023 (0.787–1.326)
Men × NA^2	**1.184 (1.026–1.353)**	1.115 (0.842–1.525)	1.109 (0.875–1.39)	0.596 (0.289–1.091)	0.857 (0.63–1.144)	0.971 (0.801–1.179)	0.985 (0.825–1.188)
Men × SI^2	1.005 (0.852–1.179)	0.811 (0.599–1.099)	1.075 (0.826–1.396)	0.673 (0.31–1.453)	0.852 (0.619–1.185)	0.925 (0.758–1.138)	0.962 (0.787–1.186)
Men × NA × SI	0.987 (0.837–1.156)	0.984 (0.666–1.426)	1.008 (0.756–1.338)	1.707 (0.825–3.538)	0.864 (0.578–1.272)	0.923 (0.706–1.191)	0.916 (0.702–1.177)
Moderating effect of age[m2]							
Age × NA	1.02 (0.902–1.15)	0.977 (0.772–1.243)	0.873 (0.747–1.027)	1.088 (0.702–1.649)	0.944 (0.705–1.334)	0.97 (0.833–1.13)	0.993 (0.839–1.175)
Age × SI	0.955 (0.849–1.059)	0.991 (0.799–1.233)	0.997 (0.848–1.196)	0.964 (0.637–1.46)	1.077 (0.87–1.342)	0.968 (0.852–1.115)	0.913 (0.799–1.041)
Age × NA^2	1.028 (0.953–1.112)	1.113 (0.97–1.278)	1.077 (0.943–1.234)	0.99 (0.729–1.37)	1.052 (0.896–1.241)	1.053 (0.946–1.173)	1.039 (0.936–1.151)
Age × SI^2	1.011 (0.935–1.099)	1.105 (0.919–1.336)	0.988 (0.864–1.141)	1.063 (0.712–1.605)	0.984 (0.811–1.205)	1.035 (0.927–1.164)	1.053 (0.937–1.188)
Age × NA × SI	0.967 (0.878–1.056)	0.952 (0.785–1.171)	1.007 (0.86–1.181)	1.001 (0.663–1.532)	0.841 (0.679–1.042)	0.96 (0.833–1.112)	0.953 (0.812–1.099)
Moderating effect of disease[m3]							
Disease × NA	1.001 (0.769–1.319)	0.97 (0.605–1.568)	1.036 (0.066–15.269)	1.085 (0.059–19.496)	1.105 (0.075–18.703)	0.937 (0.575–1.599)	0.959 (0.584–1.522)
Disease × SI	1.127 (0.852–1.534)	1.492 (0.82–2.46)	1.062 (0.077–16.481)	0.995 (0.064–16.002)	1.002 (0.064–15.805)	0.751 (0.449–1.271)	0.759 (0.462–1.213)
Disease × NA^2	0.916 (0.774–1.075)	0.908 (0.6–1.363)	1.037 (0.07–15.358)	0.979 (0.052–15.393)	0.959 (0.065–13.495)	0.94 (0.671–1.323)	0.912 (0.644–1.259)
Disease × SI^2	0.924 (0.707–1.132)	0.791 (0.532–1.162)	1.039 (0.066–15.071)	1.003 (0.062–15.562)	1.028 (0.064–16.064)	1.353 (0.952–1.946)	1.278 (0.949–1.739)
Disease × NA × SI	1.145 (0.909–1.408)	1.18 (0.737–1.873)	1.018 (0.061–16.898)	1.005 (0.061–16.547)	1.07 (0.07–18.78)	1.079 (0.62–1.825)	1.152 (0.724–1.851)

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; MACE = major adverse cardiac event; OR = odds ratio; CI = confidence interval; NA = negative affectivity; SI = social inhibition.

The 95% CI of bold cells does not include an odds ratio of 1.

[m1] = Age + Men + NA + SI + NA^2 + SI^2 + NA × SI + Men × NA + Men × SI + Men × NA^2 + Men × SI^2 + Men × NA × SI.

[m2] = Age + Men + NA + SI + NA^2 + SI^2 + NA × SI + Age × NA + Age × SI + Age × NA^2 + Age × SI^2 + Age × NA × SI.

[m3] = Age + Men + Disease + NA + SI + NA^2 + SI^2 + NA × SI + Disease × NA + Disease × SI + Disease × NA^2 + Disease × SI^2 + Disease × NA × SI.

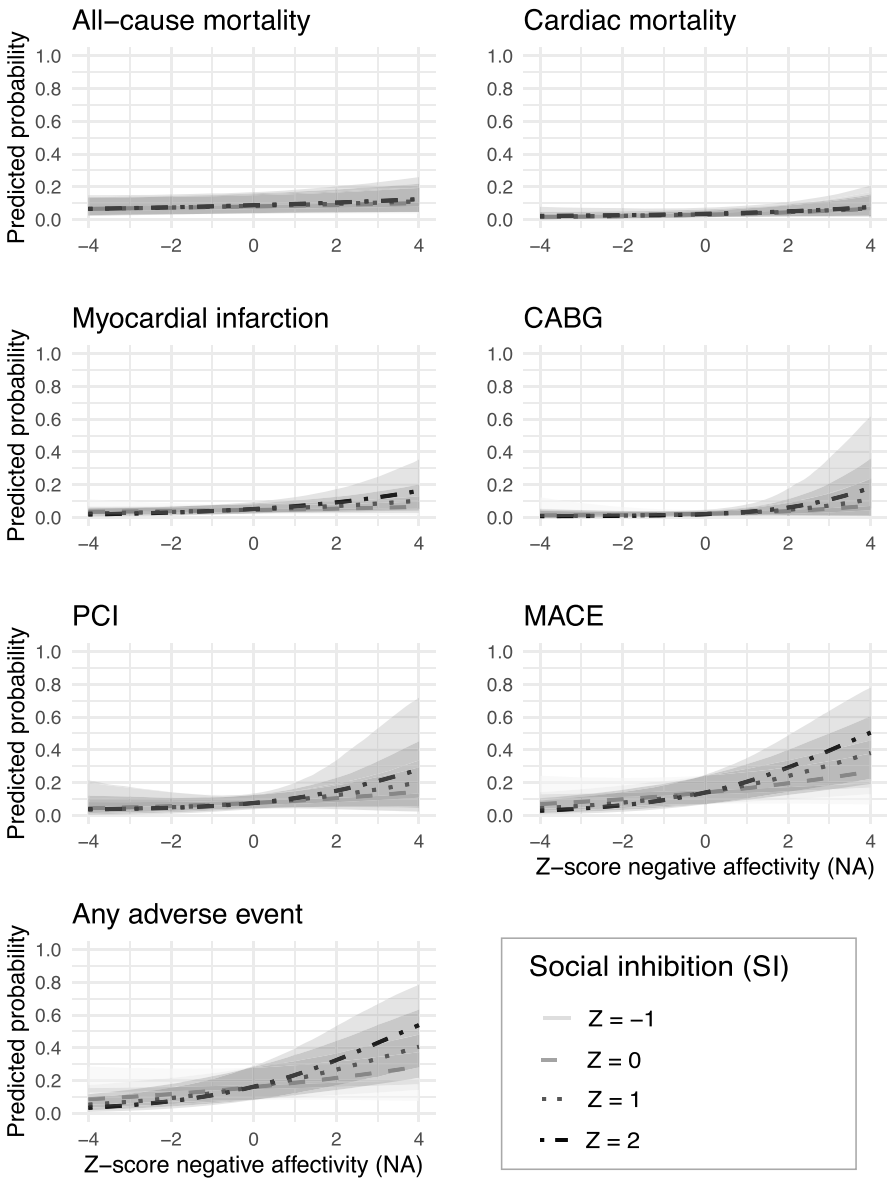

FIGURE 3. Predicted posterior probability on the occurrence of several end points during follow-up, given various scores on the standardized NA and SI scores. NA = negative affectivity; SI = social inhibition; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; MACE = major adverse cardiac event.

and outcome, the brier scores are close to zero, indicating high predictive accuracy.

DISCUSSION

We conducted an individual patient meta-analysis across 19 published prospective cohort studies investigating the prognostic effect of type D personality in patients with CVD. We estimated the type D effect according to the continuous interaction method, which performed best in several simulation studies (19,20). BFs indicated very strong evidence for the hypothesis that type D predicts the occurrence of adverse events in patients with CAD. Simple slope analysis indicated that the influence of both NA and SI on any adverse event increased across higher scores on the other personality trait. Although BFs indicated strong evidence for the type D effect on MACE, various sensitivity analyses produced 95% credible intervals containing an OR of 1, suggesting that we should entertain the possibility of no type D effect on MACE.

Evidence for a null effect was found for the outcomes all-cause mortality and cardiac mortality. The risk on those mortality end points increased with older age, male sex, and higher NA scores. A moderation of sex on a quadratic NA effect suggested that the higher NA scores increasingly resulted in a higher risk of all-cause mortality, and this pattern was more pronounced for men in comparison to women. In the subset of patients with HF, there was slightly more evidence against a type D effect on each studied end point, yet generally evidence for type D's prognostic influence in patients with HF remains inconclusive. Future research could investigate potential moderators of type D's prognostic influence on adverse events

in patients with HF, for instance, by comparing different etiologies (e.g., valvular or ischemic HF) (59).

When interpreting the type D effect on MACE and any adverse event, it is useful to inspect the effects on each of the MACE components. The type D effects on CABG, PCI, and MI are slightly smaller than the effects on MACE, and based on both the BFs and the 95% credible intervals, we cannot exclude the possibility of a null effect. Nevertheless, the type D effects on any of these individual outcomes point in the same direction, and they may have become more noticeable when combined in a composite end point such as MACE or any adverse event. One could argue that end points such as the risk on MACE or any adverse event are more interesting to patients than individual end points such as PCI or CABG, as those end points reflect a similar disease pathway, whereas their occurrence also depends on more arbitrary factors such as healthcare availability or the location of atherosclerosis.

Our finding that type D predicts adverse events in patients with CAD is in line with the conclusions drawn from earlier meta-analyses (4,5) and a reanalysis of four of the earlier studies on this topic using the continuous method (13). However, our multilevel model indicated significant differences between studies in the estimate of this type D effect. Our two-step meta-analysis reported in the supplement can reveal the studies that primarily drive this effect. The analysis indicated that all but two of the included studies showed positive estimates of the type D effect on MACE, yet the effect seems to be predominantly driven by three studies (41,42,49). Indeed, our leave-one-out meta-analysis reported in Table S5, Supplemental Digital Content, http://links.lww.com/PSYMED/A902, showed that the type D effect on MACE was no longer statistically significant when excluding one of those studies from the meta-analysis. This study involved a sample of 541 relatively young (M = 58.7) and mostly male (87%) patients with CAD (49). According to the quality assessment, there was no reason to exclude this study from our analysis. Nevertheless, our finding that the type D effect on MACE depends primarily on this particular study raises doubt on the robustness of this effect. This uncertainty is corroborated by two other observations in our statistical analysis. First, the continuous interaction model excluding the quadratic NA and SI effects did no longer show a significant interaction between NA and SI on MACE. Second, even when including those quadratic effects in the model, the 95% credible interval for the interaction between NA and SI on MACE contained one when using a flat instead of normally distributed prior for the regression coefficients. Altogether, these observations suggest that there is still uncertainty regarding the effect of type D on MACE. Nevertheless, our various sensitivity analyses all suggest an association between type D personality and adverse events in patients with CVD.

Our finding that not type D personality but only NA was associated with both all-cause and cardiac mortality contrasts with the conclusion of an earlier published meta-analysis (4). This discrepancy is likely explained by the fact that this previous meta-analysis included type D effects estimated according to the two-group method. Because this method is not able to distinguish type D effects from effects of NA or SI only (19,20), meta-analyses including such effects have the same limitation. Previous research estimated that approximately half of all published type D effects according to the two-group method were effects of NA or SI only according to the continuous method (21). Figures S1 and S2 (Supplemental Digital Content, http://links.lww.com/PSYMED/A902) show that only one of the currently included studies showed a statistically significant type D effect on all-cause and cardiac mortality according to the continuous method, whereas the earlier published meta-analysis included many studies with significant effects according to the two-group method (4). The current study suggests that many of these earlier studies showing a link between type D personality and mortality end points were in fact effects of NA only. Indeed, studies using the continuous method to estimate the type D effect have shown that only NA was associated with various outcomes, such as in-stent neoatherosclerosis (60), coronary lipid plaque (61), and medication adherence (62). Future research should use individual patient-data meta-analyses to test whether these findings are confirmed when aggregating across multiple studies.

The absence of a moderation of age on the type D effect on MACE contrasts with a previous analysis of several published studies showing that type D only predicted MACE in patients with CAD if they were younger than 70 years (22). Our moderation analysis also found no evidence that the type D effect on any outcome differs across the type of CVD. However, the confidence intervals for these moderations by disease were very wide, suggesting considerable uncertainty in these estimates. Indeed, the subgroup analyses reported in Table 3 show that the type D effects in patients with CAD are similar to those in the full sample, yet much uncertainty remains regarding the effects in patients with HF. Sex did not moderate the type D effect on any outcome, yet moderated a quadratic NA effect on all-cause mortality, suggesting that this quadratic effect differs between the sexes. The prediction model in our shiny app reveals that the risk on all-cause mortality increases quadratically with higher NA scores for male patients with CVD, whereas female patients do not show such an NA effect. This finding resonates with earlier research showing that negative mood episodes such as depression increase the mortality risk more in male than female patients (63).

Our data only allowed adjusting the type D effects for age and sex. It therefore remains unclear whether the type D effect on adverse events is confounded by other risk factors, such as lifestyle or depressive symptoms. Alternatively, these risk factors may also signify increased disease progression and therefore not confound but rather mediate or explain the association between type D personality and adverse events. Given the high correlation between NA and depressive symptoms, depression may have confounded or mediated the type D effects found in our study. Indeed, a previous meta-analysis (4) found that the overall association between type D and CVD prognosis was no longer statistically significant when limiting the analysis to the six studies that had estimated the type D effect while controlling for related psychological constructs such as symptoms of depression or anxiety. This does not necessarily imply that type D's prognostic risk is confounded by depression or anxiety symptoms, because an alternative explanation could be that mood symptoms mediate the association between type D and CAD prognosis.

We were also not able to control for other potential physical or mental morbidities that could produce both an increase in, for instance, both NA and the risk on adverse events. For these reasons, our findings do not support a *causal* influence of type D personality on adverse events. On the other hand, the studies included in our analysis that showed the largest effects of type D on adverse events (41,49) did adjust their analyses for confounders such as

decreased systolic function/left ventricular ejection fraction, exercise tolerance, and psychological stress. Nevertheless, future research could perform a highly powered preregistered investigation into the added predictive value of type D personality on adverse events in patients with CVD above and beyond the effect of depression and other clinical risk factors, while modeling type D personality according to the continuous interaction method.

Should such a high-powered preregistered analysis detect a type D effect on adverse events, then subsequent research could shed more light on the biological pathways underlying this association. Although in earlier work type D personality has been associated with impaired endothelial function (64), subclinical inflammation (65), and various inflammatory biomarkers (66,67), these analyses were based on the biased personality group methods. Future work should therefore reanalyze these studies using the continuous method to find out whether these effects were truly driven by type D personality or by an effect of NA or SI only. Recent work using the continuous method showed that type D is associated with higher levels of coronary artery calcification, after adjusting for many known CAD risk factors such as depression, smoking, diabetes, and hypertension (68). Coronary artery calcification is itself related to an increased risk of adverse cardiac events, and an unhealthy lifestyle could explain why some individuals develop high coronary artery calcification levels (69). Type D personality has been associated with less regular physical exercise (70), a less healthy diet (71), and poor self-management (72). Therefore, future research could focus on testing the role of an unhealthy lifestyle as a possible behavioral pathway mediating type D's effect on coronary artery calcification and other indicators of heart disease (12).

One clinical implication of our finding is that interventions to reduce *mortality risk* in patients with CVD should mainly target NA because elevated SI does not confer additional risk. Given the close relation between NA and other negative mood episodes such as depression, it may therefore be worthwhile to treat these patients with CVD with interventions that are effective in reducing depressive symptoms. Although a randomized controlled trial found no benefit of stepwise psychotherapy in reducing depressive symptoms in patients with CAD, a subgroup analysis revealed that the intervention was more effective in those with type D personality than in those without type D personality (46). For preventing *adverse events* in patients with CVD, it may be worthwhile to additionally intervene on SI. High SI could be reduced with, for instance, cognitive behavioral therapy (73) or acceptance and commitment therapy, allowing those with high SI to improve their emotion regulation skills (74), albeit those willing to seek help, because SI may reduce treatment-seeking behavior (75). Although SI is generally considered a temporally stable personality trait, longitudinal research has estimated that SI is 83% trait and 17% state, whereas NA is 74% trait and 26% state, suggesting that both constructs are susceptible to change (76). When individuals show increased SI due to traumatic interpersonal experiences, then targeting such experiences may potentially reduce SI and thereby its increased risk on adverse events in those with high NA.

Strengths and Limitations

Strengths of the current research are the large sample size ($N = 11{,}151$), the Bayesian estimation approach (allowing for the quantification of the evidential value for both the null and alternative hypotheses), the sensitivity analysis (one-step versus two-step individual patient-data meta-analysis), and the various contrasted type D operationalizations (two-group versus four-group versus continuous method) confirming previous work that the two-group and four-group methods cannot distinguish synergistic type D effects from main effects of NA or SI only (19,20).

Despite these strengths, our study also has several limitations. First, the cardiac mortality end point may be unreliable because identifying the cause of mortality can be difficult, particularly in elderly multimorbid patients. Second, we did not have sufficient data to adjust our estimate of the type D effect for earlier received treatments or noncardiac somatic and psychiatric diagnoses. This raises the question of whether baseline NA or SI measurements were influenced by disease- or treatment-related factors. Nevertheless, some of the studies included in this meta-analysis found significant type D effects after controlling for a history of cardiac events such as CABG, PCI, or MI (41,42,49).

Third, 7 of the 25 identified eligible studies could not be included either because of nonresponse or because of the reluctance of sharing the raw data. This resulted in excluding the potential data of 1457 patients with HF and 1035 patients with CAD. Although our analyses still involved 2027 patients with HF and 8096 patients with CAD, it was not possible to estimate a type D effect for some end points in patients with HF because of sparse data. As a result, it remains unclear whether type D is associated with an increased risk on MI, CABG, and PCI in patients with HF.

Of the seven excluded studies, two of three studies in patients with HF showed a significant association between type D personality and mortality using the two-group method (77–79). The four remaining studies focused on patients with CAD, three of which used the two-group method to show that type D personality was associated with MACE (80–82), whereas one study indicated that a cluster with patients with CAD scoring high on type D personality had an increased risk of all-cause mortality during follow-up than other patient clusters (83). None of these seven studies used the continuous method to estimate type D effects, leaving it unclear whether type D personality was driving these effects. This is likely only true for some of these studies, given that approximately half of the studies with significant type D effects based on the two-group method are effects of NA or SI only according to the continuous method (21).

Another limitation is that we did not include unpublished studies. Although one earlier meta-analysis did not find evidence of publication bias in the sample of studies investigating the MACE end point (5), another indicated that studies with smaller sample sizes showed larger type D effects than studies with larger sample sizes, possibly hinting at publication bias (4). Should it be the case that there exist unpublished studies investigating the risk of type D on adverse events in patients with CVD and that those studies differ from published studies in their effect sizes, then publication bias may have affected our conclusions.

Our meta-analysis was applied to total NA and SI scores because individual item scores were no longer available for various studies included in our analysis. Therefore, we were not able to conduct item-level analyses, testing whether specific combinations of NA and SI items interact in predicting adverse events. We recommend researchers in future studies on type D personality to test item-level interaction effects to investigate which items primarily drive a potential significant interaction effect between NA and SI.

Because of the lack of individual item scores, we were not able to conduct an item response theory-based measurement harmonization to link the differently sized DS14 and DS16 scales. As a workaround, we standardized the NA and SI total scores to the same *z*-score metric. We were also not able to determine whether the measurement instruments showed signs of differential item functioning across the included studies. Nevertheless, previous research using item response theory has shown that the DS14 instrument provides fairly comparable measurements across the general and clinical populations (84). Future research could investigate this measurement invariance across other factors such as age, sex, or type of CVD.

CONCLUSIONS

In light of recent findings that a major part of the published type D effects may be false positives masquerading for effects of NA or SI only (19–21), our study is a first endeavor at a large-scale reanalysis of the published type D literature. Using the continuous method, our reanalysis suggests that some of the earlier published type D effects on all-cause and cardiac mortality (16,39) are likely effects of NA only. Nevertheless, based on this individual patient-data meta-analysis of 19 published prospective cohort studies, type D personality poses an increased risk on the occurrence of adverse events in patients suffering from CAD.

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REFERENCES

1. Denollet J. DS14: standard assessment of negative affectivity, social inhibition, and type D personality. Psychosom Med 2005;67:89–97.
2. Denollet J. Type D personality: a potential risk factor refined. J Psychosom Res 2000;49:255–66.
3. Denollet J. Personality and coronary heart disease: the type-D scale-16 (DS16). Ann Behav Med 1998;20:209–15.
4. Grande G, Romppel M, Barth J. Association between type D personality and prognosis in patients with cardiovascular diseases: a systematic review and meta-analysis. Ann Behav Med 2012;43:299–310.
5. O'Dell KR, Masters KS, Spielmans GI, Maisto SA. Does type-D personality predict outcomes among patients with cardiovascular disease? A meta-analytic review. J Psychosom Res 2011;71:199–206.
6. Versteeg H, Spek V, Pedersen SS, Denollet J. Type D personality and health status in cardiovascular disease populations: a meta-analysis of prospective studies. Eur J Prev Cardiol 2012;19:1373–80.
7. Horsten M, Erigson M, Perski A, Wamala SP, Schenck-Gustafsson K, Orth-Gomér K. Psychosocial factors and heart rate variability in healthy women. Psychosom Med 1999;61:49–57.
8. Brosschot JF, Thayer JF. Anger inhibition, cardiovascular recovery, and vagal function: a model of the link between hostility and cardiovascular disease. Ann Behav Med 1998;20:326–32.
9. Matthews KA, Owens JF, Kuller LH, Sutton-Tyrrell K, Jansen-McWilliams L. Are hostility and anxiety associated with carotid atherosclerosis in healthy postmenopausal women? Psychosom Med 1998;60:633–8.
10. Parker G, Malhi G, Mitchell P, Wilhelm K, Austin MP, Crawford J, et al. Progressing a spectrum model for defining non-melancholic depression. Acta Psychiatr Scand 2005;111:139–43.
11. Coyne JC, de Voogd JN. Are we witnessing the decline effect in the type D personality literature? What can be learned? J Psychosom Res 2012;73:401–7.
12. Kupper N, Denollet J. Type D personality as a risk factor in coronary heart disease: a review of current evidence. Curr Cardiol Rep 2018;20:104.
13. Kupper N, Denollet J. Explaining heterogeneity in the predictive value of type D personality for cardiac events and mortality. Int J Cardiol 2016;224:119–24.
14. Kupper N, Denollet J. Type D personality as a prognostic factor in heart disease: assessment and mediating mechanisms. J Pers Assess 2007;89:265–76.
15. Pedersen SS, Denollet J. Type D personality, cardiac events, and impaired quality of life: a review. Eur J Cardiovasc Prev Rehabil 2003;10:241–8.
16. Denollet J, Sys SU, Brutsaert DL. Personality and mortality after myocardial infarction. Psychosom Med 1995;57:582–91.
17. Ferguson E, Williams L, O'Connor RC, Howard S, Hughes BM, Johnston DW, et al. A taxometric analysis of type-D personality. Psychosom Med 2009;71:981–6.
18. Smith TW. Toward a more systematic, cumulative, and applicable science of personality and health: lessons from type D personality. Psychosom Med 2011;73:528–32.
19. Lodder P. Modeling synergy: how to assess a type D personality effect. J Psychosom Res 2020;132:109990.
20. Lodder P. A re-evaluation of the type D personality effect. Pers Individ Dif 2020; 167:110254.
21. Lodder P, Kupper N, Antens M, Wicherts JM. A systematic review comparing two popular methods to assess a type D personality effect. 2021;71:62–75.
22. Belzak WCM, Bauer DJ. Interaction effects may actually be nonlinear effects in disguise: a review of the problem and potential solutions. Addict Behav 2019;94:99–108.
23. Lodder P, Denollet J, Emons WHM, Nefs G, Pouwer F, Speight J, et al. Modeling interactions between latent variables in research on type D personality: a Monte Carlo simulation and clinical study of depression and anxiety. Multivariate Behav Res 2019;54:637–65. doi:10.1080/00273171.2018.1562863.
24. Lodder P, Emons WHM, Denollet J, Wicherts JM. Latent logistic interaction modeling: a simulation and empirical illustration of type D personality. Struct Equ Model 2021;28:440–62.
25. Park C, Won MH, Son YJ. Mediating effects of social support between type D personality and self-care behaviours among heart failure patients. J Adv Nurs 2021;77:1315–24.
26. Tak LM, Meijer A, Manoharan A, de Jonge P, Rosmalen JG. More than the sum of its parts: meta-analysis and its potential to discover sources of heterogeneity in psychosomatic medicine. Psychosom Med 2010;72:253–65.
27. Riordan AO, Howard S, Gallagher S. Social context and sex moderate the association between type D personality and cardiovascular reactivity. Appl Psychophysiol Biofeedback 2019;44:321–30.
28. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med 2013;158:280–6.
29. Enders CK, Tofighi D. Centering predictor variables in cross-sectional multilevel models: a new look at an old issue. Psychol Methods 2007;12:121–38.
30. Ferreira-González I, Permanyer-Miralda G, Domingo-Salvany A, Busse JW, Heels-Ansdell D, Montori VM, et al. Problems with use of composite end points in cardiovascular trials: systematic review of randomised controlled trials. BMJ 2007;334:786.
31. Burke DL, Ensor J, Riley RD. Meta-analysis using individual participant data: one-stage and two-stage approaches, and why they may differ. Stat Med 2017; 36:855–75.
32. Bürkner PC. brms: an R package for Bayesian multilevel models using Stan. J Stat Softw 2017;80. doi:10.18637/jss.v080.i01.
33. van Zwet E. A default prior for regression coefficients. Stat Methods Med Res 2019;28:3799–807.
34. Verdinelli I, Wasserman L. Computing Bayes factors using a generalization of the Savage-Dickey density ratio. J Am Stat Assoc 1995;90:614–8.
35. Kass RE, Raftery AE. Bayes factors. J Am Stat Assoc 1995;90:773–95.
36. Riley RD, Lambert PC, Abo-Zaid G. Meta-analysis of individual participant data: rationale, conduct, and reporting. BMJ 2010;340:521–5.
37. Rice K, Higgins JPT. A re-evaluation of fixed effect(s) meta-analysis. J R Stat Soc Ser B Stat Methodol 2018;181:205–27.
38. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2017.
39. Denollet J, Sys SU, Stroobant N, Rombouts H, Gillebert TC, Brutsaert DL. Personality as independent predictor of long-term mortality in patients with coronary heart disease. Lancet 1996;347:417–21.
40. 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;102:630–5.
41. Denollet J, Pedersen SS, Vrints CJ, Conraads VM. Usefulness of type D personality in predicting five-year cardiac events above and beyond concurrent symptoms of stress in patients with coronary heart disease. Am J Cardiol 2006;97:970–3.
42. 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;71:778–83.
43. Pelle AJ, Pedersen SS, Schiffer A, Fail CH. Psychological distress and mortality in systolic heart failure. Circ Heart Fail 2010;3:261–7.
44. Schmidt MM, Quadros AS, Abelin AP, Minozzo EL, Wottrich SH, Kunert HZ, et al. Psychological characteristics of patients undergoing percutaneous coronary interventions. Arq Bras Cardiol 2011;97:331–7.
45. Coyne JC, Jaarsma T, Luttik M-L, van Sonderen E, van Veldhuisen DJ, Sanderman R. Lack of prognostic value of type D personality for mortality in a large sample of heart failure patients. Psychosom Med 2011;73:557–62.
46. Herrmann-Lingen C, Beutel ME, Bosbach A, Deter HC, Fritzsche K, Hellmich M, et al. A stepwise psychotherapy intervention for reducing risk in coronary artery disease (SPIRR-CAD): results of an observer-blinded, multicenter, randomized trial in depressed patients with coronary artery disease. Psychosom Med 2016;78:704–15.
47. Grande G, Romppel M, Vesper J-M, Schubmann R, Glaesmer H, Herrmann-Lingen C. Type D personality and all-cause mortality in cardiac patients—data from a German cohort study. Psychosom Med 2011;73:548–56.
48. Denollet J, Tekle FB, Pedersen SS, van der Voort PH, Alings M, van den Broek KC. Prognostic importance of distressed (type D) personality and shocks in patients with an implantable cardioverter defibrillator. Int J Cardiol 2013;167:2705–9.

49. Denollet J, Pedersen SS, Vrints CJ, Conraads VM. Predictive value of social inhibition and negative affectivity for cardiovascular events and mortality in patients with coronary artery disease: the type D personality construct. Psychosom Med 2013;75:873–81.
50. Meyer T, Hussein S, Lange HW, Herrmann-Lingen C. Type D personality is unrelated to major adverse cardiovascular events in patients with coronary artery disease treated by intracoronary stenting. Ann Behav Med 2014;48:156–62.
51. Sumin AN, Raikh OI, Gaifulin RA, Korok EV, Bezdenezhnykh AV, Ivanov SV, et al. Predisposition to psychological distress in patients after coronary bypass surgery: relation to one year prognosis. Kardiologiia 2015;55:76–82.
52. Dulfer K, Hazemeijer BA, Van Dijk MR, Van Geuns RJ, Daemen J, Van Domburg RT, et al. Prognostic value of type D personality for 10-year mortality and subjective health status in patients treated with percutaneous coronary intervention. J Psychosom Res 2015;79:214–21.
53. Gostoli S, Bonomo M, Roncuzzi R, Biffi M, Boriani G, Rafanelli C. Psychological correlates, allostatic overload and clinical course in patients with implantable cardioverter defibrillator (ICD). Int J Cardiol 2016;220:360–4.
54. Pushkarev GS, Kuznetsov VA, Yaroslavskaya EI, Bessonov IS. Prognostic significance of psychosocial risk factors in patients with ischemic heart disease after percutaneous coronary interventions. Kardiologiya 2017;57:11–5.
55. Conden E, Rosenblad A, Wagner P, Leppert J, Ekselius L, Aslund C. Is type D personality an independent risk factor for recurrent myocardial infarction or all-cause mortality in post-acute myocardial infarction patients? Eur J Prev Cardiol 2017;24:522–33.
56. Lin T-K, You K-X, Hsu C-T, Li YD, Lin CL, Weng CY, et al. Negative affectivity and social inhibition are associated with increased cardiac readmission in patients with heart failure: a preliminary observation study. PLoS One 2019;14:e0215726. doi:10.1371/journal.pone.0215726.
57. Lv H, Tao H, Wang Y, Zhao Z, Liu G, Li L, et al. Impact of type D personality on major adverse cardiac events in patients undergoing percutaneous coronary intervention: the mediating role of cognitive appraisal and coping style. J Psychosom Res 2020;136:110192.
58. Kruschke J. Doing Bayesian data analysis: a tutorial with R, JAGS, and Stan. 1st ed. Cambridge, MA: Elsevier Academic Press; 2010
59. Kobayashi M, Voors AA, Girerd N, Billotte M, Anker SD, Cleland JG, et al. Heart failure etiologies and clinical factors precipitating for worsening heart failure: findings from BIOSTAT-CHF. Eur J Intern Med 2020;71:62–9.
60. Lee R, Yu H, Gao X, Cao J, Tao H, Yu B, et al. The negative affectivity dimension of type D personality is associated with in-stent neoatherosclerosis in coronary patients with percutaneous coronary intervention: an optical coherence tomography study. J Psychosom Res 2019;120:20–8.
61. Wang Y, Zhao Z, Gao X, Li L, Liu G, Chen W, et al. Type D personality and coronary plaque vulnerability in patients with coronary artery disease: an optical coherence tomography study. Psychosom Med 2016;78:583–92.
62. Wu JR, Moser DK. Type D personality predicts poor medication adherence in patients with heart failure in the USA. Int J Behav Med 2014;21:833–42.
63. Gilman SE, Sucha E, Kingsbury M, Horton NJ, Murphy JM, Colman I. Depression and mortality in a longitudinal study: 1952–2011. CMAJ 2017;189:E1304–10.
64. Denollet J, van Felius RA, Lodder P, Mommersteeg PM, Goovaerts I, Possemiers N, et al. Predictive value of type D personality for impaired endothelial function in patients with coronary artery disease. Int J Cardiol 2018;259:205–10.
65. van Dooren FE, Verhey FR, Pouwer F, Schalkwijk CG, Sep SJ, Stehouwer CD, et al. Association of type D personality with increased vulnerability to depression: is there a role for inflammation or endothelial dysfunction?—the Maastricht study. J Affect Disord 2016;189:118–25.
66. Conraads VM, Denollet J, De Clerck LS, Stevens WJ, Bridts C, Vrints CJ. Type D personality is associated with increased levels of tumour necrosis factor (TNF)-alpha and TNF-alpha receptors in chronic heart failure. Int J Cardiol 2006;113:34–8.
67. Denollet J, Schiffer AA, Kwaijtaal M, Hooijkaas H, Hendriks EH, Widdershoven JW, et al. Usefulness of type D personality and kidney dysfunction as predictors of interpatient variability in inflammatory activation in chronic heart failure. Am J Cardiol 2009;103:399–404.
68. Raykh OI, Sumin AN, Kokov AN, Indukaeva EV, Artamonova GV. Association of type D personality and level of coronary artery calcification. J Psychosom Res 2020;139:110265.
69. Liu W, Zhang Y, Yu CM, Ji QW, Cai M, Zhao YX, et al. Current understanding of coronary artery calcification. J Geriatr Cardiol 2015;12:668–75.
70. Bunevicius A, Brozaitiene J, Staniute M, Gelziniene V, Duoneliene I, Pop VJ, et al. Decreased physical effort, fatigue, and mental distress in patients with coronary artery disease: importance of personality-related differences. Int J Behav Med 2014;21:240–7.
71. Booth L, Williams L. Type D personality and dietary intake: the mediating effects of coping style. J Health Psychol 2015;20:921–7.
72. Kessing D, Denollet J, Widdershoven J, Kupper N. Self-care and health-related quality of life in chronic heart failure: a longitudinal analysis. Eur J Cardiovasc Nurs 2017;16:605–13.
73. Ludwig LD, Lazarus AA. A cognitive and behavioral approach to the treatment of social inhibition. Psychother Theory Res Pract 1972;9:204.
74. Forman EM, Herbert JD, Moitra E, Yeomans PD, Geller PA. A randomized controlled effectiveness trial of acceptance and commitment therapy and cognitive therapy for anxiety and depression. Behav Modif 2007;31:772–99.
75. Pati S, Hussain MA, Chauhan AS, Mallick D, Nayak S. Patient navigation pathway and barriers to treatment seeking in cancer in India: a qualitative inquiry. Cancer Epidemiol 2013;37:973–8.
76. Lodder P, Kupper N, Mols F, Emons WH, Wicherts JM. Assessing the temporal stability of psychological constructs: an illustration of type D personality, anxiety and depression. J Res Pers 2022;104299:104299.
77. Bundgaard JS, Østergaard L, Gislason G, Thune JJ, Nielsen JC, Haarbo J, et al. Association between type D personality and outcomes in patients with non-ischemic heart failure. Qual Life Res 2019;28:2901–8.
78. Denollet J, Holmes RV, Vrints CJ, Conraads VM. Unfavorable outcome of heart transplantation in recipients with type D personality. J Heart Lung Transplant 2007;26:152–8.
79. Volz A, Schmid JP, Zwahlen M, Kohls S, Saner H, Barth J. Predictors of readmission and health related quality of life in patients with chronic heart failure: a comparison of different psychosocial aspects. J Behav Med 2011;34:13–22.
80. Du J, Zhang D, Yin Y, Zhang X, Li J, Liu D, et al. The personality and psychological stress predict major adverse cardiovascular events in patients with coronary heart disease after percutaneous coronary intervention for five years. Medicine (Baltimore) 2016;95:e3364.
81. Imbalzano E, Vatrano M, Quartuccio S, Ceravolo R, Ciconte VA, Rotella P, et al. Effect of type D personality on smoking status and their combined impact on outcome after acute myocardial infarction. Clin Cardiol 2018;41:321–5.
82. Leu HB, Yin WH, Tseng WK, Wu YW, Lin TH, Yeh HI, et al. Impact of type D personality on clinical outcomes in Asian patients with stable coronary artery disease. J Formos Med Assoc 2019;118:721–9.
83. Modica M, Carabalona R, Spezzaferri R, Tavanelli M, Torri A, Ripamonti V, et al. Psychological profiles derived by cluster analysis of Minnesota Multiphasic Personality Inventory and long term clinical outcome after coronary artery by pass grafting. Monaldi Arch Chest Dis 2012;78:29–33.
84. Emons WH, Meijer RR, Denollet J. Negative affectivity and social inhibition in cardiovascular disease: evaluating type-D personality and its assessment using item response theory. J Psychosom Res 2007;63:27–39.