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Modeling synergy: How to assess a Type D personality effect

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ABSTRACT

Objective: In research on Type D personality, its subcomponents negative affectivity (NA) and social inhibition (SI) are hypothesized to have a synergistic effect on various medical and psychosocial outcomes. As some methods to analyze Type D personality have been criticized, this study investigated whether these methods adequately detect a Type D effect.

Method: We used a simulation and two empirical illustrations to investigate each method's performance (bias, power and false positives) in detecting the Type D effect.

Results: Our simulation showed that the two most commonly used methods to assess the Type D effect (subgroup methods) were primarily picking up the presence of NA or SI main effects, indicating that these methods might falsely suggest synergistic Type D effects. Moreover, these methods failed to detect the *combined* presence of the NA and SI main effects, resulting in significant Type D effects when only one of the NA/SI main effects was present. The method that best detected Type D effects modeled the continuous NA/SI main effects and their statistical interaction in a regression analysis. Reanalysis of two empirical Type D personality datasets confirmed the patterns found in our simulation.

Conclusion: This study showed that Type D effects should be modeled with a continuous interaction approach. Other approaches showed either more bias, more false positive findings or lower power. We recommend against using subgroup approaches to operationalize Type D personality, as these methods are biased, regardless of whether the Type D effect is synergistic or additive in nature.

1. Introduction

Scientific models are often multidimensional, where variation in a particular quantitative or qualitative outcome is explained by more than one predictor. There are several ways to conceptualize the relation between two predictors and one outcome. For instance, one predictor can confound, mediate, or moderate the association between the other predictor and the outcome (see [1] for a review). The focus of the present article is a specific type of moderating effect, called synergy.

Two predictors synergistically influence an outcome when their effect is more than the sum of their parts. As such, the *combined* influence of these predictors has to be captured by the statistical model. This does *not* mean summing the two predictor effects in an additive model, because then their combined effect would not be more than the sum of their parts. However, synergy *can* be taken into account by adding to the model an interaction effect between the two predictors. For concluding a synergistic effect, a significant interaction is necessary

but not sufficient. An additional requirement is that the interaction effect is in the same direction as the main effects, so that the positive (or negative) effect of one predictor on an outcome gets more positive (or negative) with higher scores on the other predictor.

1.1. Type D personality

Research on Type D personality arguably serves as a perfect case study for modeling synergy [2]. People with a Type D (Distressed) personality type score high on the two personality traits negative affectivity (NA) and social inhibition (SI). People with negative affectivity have a tendency to experience negative thoughts and behaviors and socially inhibited persons have difficulty expressing their thoughts and emotions, especially in social situations [3]. It is the *combined* presence of both personality traits that has been found as a risk factor for various outcomes, suggesting a synergistic effect [2]. Earlier writings on Type D personality suggested that the Type D effect is *more* than additive. For

Abbreviations: NA, Negative affectivity; SI, Social inhibition

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instance, Kupper & Denollet [4] explicitly stated that Type D personality is a synergy between NA and SI (see also [5], p. 245). Furthermore, Denollet, Sys and Brutsaert [6] claimed that the *interaction* [emphasis added] 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). Similarly, Denollet and colleagues [7,8] more than once suggest that social inhibition *modulates* [emphasis added] the effect of negative emotions on cardiac prognosis. These findings point to a synergistic Type D.

Type D personality has been associated with various adverse medical and psychosocial outcomes. For instance, a systematic review showed people with Type D personality to have a 3-fold increased risk on cardiac events compared to people with no Type D personality [9]. Furthermore, in a population of patients with cardiovascular disease, a meta-analysis concluded that Type D's show a higher all-cause mortality than non Type D's [10]. However, the size of these effects appeared to decrease over time because more recent studies [11–13] failed to corroborate earlier findings. Some have argued that these inconsistencies can in part be explained by the different approaches used to operationalize the Type D effect [2,14,15]. We now turn to a discussion of each of those methods.

1.2. How to assess the Type D effect?

Though in earlier work we showed how latent variable methods are very useful alternatives in modeling a Type D effect [16], for the purpose of the present discussion we focus on methods that do not specify a measurement model (also called observed score methods), as these are most commonly used in the Type D literature. Though observed score methods are relatively easy to model, they fail to consider measurement error in the item scores or other aspects of the measurement model.

To the best of our knowledge, four operationalizations of Type D personality have been reported in the literature. Table 1 shows an example dataset required to operationalize Type D personality using each of the four methods. NA and SI, the two traits underlying Type D personality, are each measured with seven items on a 0 to 4 Likert scale in the DS14 questionnaire [17]. The four methods have in common that the seven item scores measuring each construct are first summed, resulting in NA and SI sum scores ranging from 0 to 28. However, from this point onwards the methods start to diverge.

The two most widely used methods first dichotomize the NA and SI sum scores using a fixed cutoff score of 10, to indicate whether people score high or low on the NA and SI traits (NA+ and SI+ in Table 1). Though IRT analyses suggested that the NA and SI traits are most reliably measured around the cutoff score [18], others have questioned the validity of the assumptions underlying that analysis [14]. In any case, all people who score above the predetermined cutoff on both traits are assumed to have a Type D personality (NA+ SI+ in Table 1). Similarly, three other classifications can be made using the two dichotomized NA and SI scores: people scoring high on NA and low on SI (NA+ SI-); low on NA and high on SI (NA- SI+); low on NA and SI (NA- SI-).

Table 1
Example of data required to analyze Type D personality according to four methods.

ID	NA	SI	NA+	SI+	NA+ SI+	NA+ SI-	NA- SI+	NA- SI-	NAC	SIC	NAC * SIC
1	20	17	1	1	1	0	0	0	8	7	56
2	7	9	0	0	0	0	0	1	-5	1	5
3	18	3	1	0	0	1	0	0	6	-7	-42
4	5	12	0	1	0	0	1	0	-7	2	-14
5	10	9	1	0	0	1	0	0	-2	-1	2

NA = negative affectivity sum score; SI = social inhibition sum score; NA+ = NA score above cutoff; SI+ = SI score above cutoff; NA- SI- = NA and SI score below cutoff; NA+ SI- = NA score above, and SI score below cutoff; NA- SI+ = NA score below, and SI score above cutoff; NA+ SI+ = NA and SI score above cutoff (Type D group); NAC = mean centered NA score; SIC = mean centered SI score; NAC * SIC = multiplication of mean centered NA and SI scores.

1.2.1. 2-group approach

The first method used to assess Type D's synergistic effect is called the 2-group approach and includes the dichotomous NA+ SI+ variable as a predictor in a regression model. This method estimates the effect of people who score high on both constructs versus people who do not score high on both constructs. Despite being the most commonly used operationalization, Smith [2] has argued that the 2-group approach does not appropriately assess a synergistic effect, as such a 2-group effect could also result from patterns other than synergy. For instance, if in reality there exists *only* a main effect for NA on some outcome, then comparing a Type D group (NA+ SI+) with a non Type D group (NA+ SI-, NA- SI+, NA- SI-) will result in false positive Type D effects for the following reason. Both the Type D and non-Type D group contain a high-risk group of people with high NA scores (NA+ SI+ vs. NA+ SI-). However, in the non Type D group the effect of the high-risk group (NA+ SI-) is averaged with that of the two low risk groups (NA- SI+ & NA- SI-). By not taking into account the NA and SI main effects, we expect the 2-group approach to be biased in assessing the synergistic Type D effect.

1.2.2. 4-group approach

The second method is called the 4-group approach and includes the NA+ SI+, NA+ SI- and NA- SI+ variables as predictors in a dummy-coded regression model. In this way the effect of each of these three dummy variables is estimated relative to that of the reference group NA- SI-. This 4-group approach is expected to show larger Type D effects than the 2-group approach when focusing on the contrast of the Type D group with the lowest risk group only (see for instance 13), while for the 2-group approach Type D is contrasted with the three non Type D groups combined. Note that in practice, researchers sometimes apply a stricter criterion before concluding a significant Type D effect based on the 4-group approach, where the Type D group needs to show a significant effect relative to *each* of the three other groups separately.

1.2.3. Continuous interaction approach

The third operationalization of Type D personality has been advocated by various critics as the method of choice [2,15,16,21]. This *continuous interaction* approach includes both the NA and SI sum scores, as well as their interaction term in a regression model. When constructing the interaction term, the sum scores are typically mean-centered before multiplying them (NAC, SIC, NAC * SIC in Table 1). The continuous interaction approach differs from the three other operationalizations in that it uses the NA and SI sum scores, rather than their dichotomized values. This is also the main reason the critics prefer this approach above the others. Various authors have argued against the practice of dichotomizing continuous variables, not only because it reduces the power in statistical tests [20,22], but also because under some circumstances it increases the risk on spurious findings [23–25]. For instance, if predictors A and B are correlated and only predictor A has an effect on an outcome, then dichotomizing both predictors before including them in a regression model results in an increased false positive rate for predictor B and for the interaction between A and B [26]. Dichotomizing two correlated continuous predictors also causes a

failure to distinguish non-linear (e.g. quadratic) from interaction effects in regression models [27,28]. In the context of research on Type D personality, because the continuous NA and SI scores typically show a moderate correlation ($r = 0.5$), critics have argued against using approaches based on dichotomized NA and SI variables [2,16].

1.2.4. Adjusted 2-group approach

As opposed to the first three approaches, the fourth operationalization of Type D personality is almost never used in practice (see [14] for an exception). This approach is similar to the continuous interaction approach, but models the dichotomized instead of continuous NA and SI scores, resulting in less statistical power to detect the Type D effect. Interestingly, when multiplying the dichotomized NA and SI scores, the resulting interaction term is exactly the same as the dichotomous Type D variable in the 2-group approach (NA+ SI+). However, the current method differs from the regular 2-group approach because it adjusts this interaction for the (dichotomized) main effects of NA and SI. Because the regular 2-group approach does not include these dichotomized main effects in regression analyses, it can be considered a dichotomous interaction model without main effects, a practice argued against in many introductory statistical textbooks (e.g. 20). Because this fourth method does adjust the Type D effect for the dichotomized NA and SI main effects, we call it the *adjusted 2-group* approach.

1.3. Conflicting Type D results

Several studies have reported the effect of Type D personality on some outcome measure, using more than one operationalization of Type D personality. Some of these studies showed significant effects for the 2-group approach, while the continuous interaction approach failed to reach significance. For instance, Dulfer and colleagues [30] reported based on the 2-group approach that people with Type D personality had a larger odds on all-cause mortality than people without Type D personality (OR = 1.58, 95%CI = 1.22, 2.03), while the effect according to the continuous interaction approach failed to reach significance (OR = 0.95, 95%CI = 0.78, 1.17). An imaging study by Wang and colleagues [31] showed that Type D's, compared to non Type D's, were at increased odds of having lipid artery plaque according to the 2-group approach (OR = 4.87, 95%CI = 1.41, 11.14), while the effect based on the continuous interaction approach did not reach significance (OR = 0.66, 95%CI = 0.17, 2.51). Further research by Wang and colleagues [32] reported that Type D's, compared to non Type D's, were at increased odds of having In-stent restenosis (OR = 2.82, 95%CI = 1.26, 6.3) according to the 2-group approach, while the continuous interaction approach did not show such a significant effect (OR = 1.13, 95%CI = 0.45, 3.10). Lastly, Williams, O'Connor, Grubb and Carroll [33] reported based on the 2-group approach that people with Type D personality had a lower quality of life compared to non Type D's ($d = -1.52$, 95%CI = -1.86, -1.19), while the effect according to the continuous interaction approach failed to reach significance.

A limitation of these reports, however, is that the effect sizes (e.g. odds ratios) were not calculated using predictors on a standardized scale, making it difficult to compare them in size. Nevertheless, p -values are not affected by the standardization process and these indicate that the dichotomous approaches are statistically significant while the continuous interaction approaches are not.

Taken together, these findings stress the importance of assessing the consequences of using different operationalizations of synergistic effects such as Type D personality. Given that in earlier studies on Type D reported above, the conclusions were conditional on the chosen operationalization of Type D, it is paramount to uncover which of these methods accurately detect a true Type D effect. In the present study we aim to answer this question by using both a Monte Carlo simulation, as well as a reanalysis of earlier published data investigating the link between Type D personality and various medical outcomes. The

simulation study enables us to directly test Smith's [2] conjecture that the 2-group approach does not adequately detect a (synergistic) Type D effect, but is also sensitive to the mere presence of NA or SI main effects.

2. Method

2.1. Procedure

In our simulation study we generated 75,000 datasets to test the association between Type D personality and cardiac events under varying circumstances. We varied these simulated datasets across two parameters: [1] the size of the NA & SI main effects on cardiac events (odds ratio = 0.8, 0.85, 0.9, 0.95, 1.00, 1.05, 1.10, 1.15, 1.20, 1.25, 1.30, 1.35, 1.40, 1.45, 1.50) and [2] the size of the NA & SI interaction effect on cardiac events (odds ratio = 0.50, 0.75, 1.00, 1.25, 1.50), resulting in $15 * 5 = 75$ different simulation conditions. In each of these 75 conditions we generated 1000 datasets, where each dataset contained for 500 participants the DS14 item scores and a simulated dichotomous outcome.

In the second step of our simulation study we analyzed each of those 45,000 datasets according to the four Type D personality operationalizations. Within each condition we aggregated the results of the 1000 replications by averaging the estimated Type D effects and by computing the percentage of statistically significant effects. To assess the performance of each method, we reported the absolute and relative bias in the estimated Type D effects, as well as the percentage of significant Type D effects. The latter allowed us to determine both the statistical power and the percentage of false positives in detecting a Type D effect. Note that for all approaches, slight negative bias in the estimated Type D effects was expected because all approaches do not take into account the measurement error in the NA and SI item scores.

2.2. Data generation

As formula 1 shows, the data generating mechanism in this simulation study was a latent logistic interaction model, where a dichotomous outcome (cardiac events) is regressed on the latent variables NA (ξ_1) and SI (ξ_2), and their interaction ($\xi_1\xi_2$):

$$\ln\left(\frac{p(\xi)}{1-p(\xi)}\right) = \beta_1\xi_1 + \beta_2\xi_2 + \beta_3\xi_1\xi_2 \quad (1)$$

This regression model contained three parameters: one regression coefficient for the main effect of the latent NA construct (β_1), one for the main effect of the latent SI construct (β_2), and one for the interaction between the latent NA and SI constructs (β_3). The magnitudes of these regression coefficients were varied across the 45 simulation conditions.

The latent NA and SI constructs both followed a bivariate standard normal distribution with a mean vector of zero and correlation matrix: $(\xi_1, \xi_2) \sim \mathcal{N}(0, \Sigma)$, $\Sigma = \begin{bmatrix} 1 & 0.5 \\ 0.5 & 1 \end{bmatrix}$. These latent NA and SI scores were used to simulate continuously distributed DS14 item scores based on a standard two factor model, with the seven factor loadings of NA and SI ranging between 0.7 and 0.8, corresponding to an estimated Cronbach's alpha of 0.89 for NA and 0.86 for SI. For all items the intercepts were fixed at -0.9 in order to maintain a prevalence of Type D personality of approximately 25%. The resulting 14 continuous item scores were transformed to 14 ordinal item scores on a 0–4 Likert scale, using four threshold parameters (Muthén & Kaplan's [34] Case 1 thresholds: $[-1.645, -0.643, 0.643, 1.645]$). For the purpose of a sensitivity analysis we transformed the continuous item scores to *positively skewed* ordinal item scores using a different set of threshold parameters (Muthén & Kaplan's [34] Case 3 thresholds: $[-0.05, 0.772, 1.341, 1.881]$).

In the last step of the data generation, for each participant a cardiac event score was drawn from a binomial distribution with a probability resulting from filling in formula one the participant's latent NA and SI

score, as well as the three regression coefficients that varied across the simulation conditions. For the purpose of another sensitivity analysis, scores on an observed *continuous* outcome were generated by filling in formula one (without the logit link function) and by adding a random error term with mean zero and variance one.

2.3. Data analysis

For every simulation condition, each of the 1000 datasets was analyzed using the four Type D operationalizations. A binary logistic regression model was used for the dichotomous outcomes, while a linear regression model was used for continuous outcomes. The regression terms were specified based on the description in the synergy assessment section. In the main simulation, the Type D effect according to the 4-group approach was investigated using the contrast between the Type D group and the reference group with low scores on both NA and SI. An additional simulation was conducted investigating for the 4-group approach the contrasts of the Type D group with all three other groups separately. In this simulation, the correlation between NA and SI was varied (0 or 0.5) because this will illustrate why the 4-group approach did not perform adequately in detecting Type D effects.

In the analyzed logistic regression models, the estimated regression coefficients were standardized by multiplying the unstandardized coefficients with the standard deviation of the predictor variable [35], and subsequently exponentiated to compute the odds ratio. For continuous outcomes, the regression coefficients were standardized by multiplying with the standard deviation of the predictor divided by the standard deviation of the continuous outcome.

In each condition, the estimated effects were averaged across the 1000 replications. The absolute bias was determined by subtracting from this average the true condition specific Type D effect. The relative bias was determined by dividing the absolute bias by the true condition specific Type D effect. The percentage of significant effects was calculated by dividing the total number of significant effects in a condition by 1000 (replications) and multiplying by 100%. The R-script of this simulation can be found on this project's open science framework page: <https://osf.io/qdgrk/>.

3. Results

3.1. Main simulation results

Fig. 1 shows the results of our simulation study according to three outcome measures: mean estimated Type D effect (top row), relative bias (center row) and percentage of significant effects (bottom row). The three columns represent varying sizes of the Type D effect, where the effect is absent in the first column and positively increasing in the second and third columns. In each plot the outcome measure (y-axis) is plotted against the size of the NA/SI main effects (x-axis). Note that the scale of these main effects is standardized. A main effect of 1.2 implies that people with average NA/SI scores, show a 1.2 larger odds on an events, than people scoring one standard deviation below average on NA and SI. Lastly, in all plots each line has its own color and type, representing the different approaches to operationalize the synergistic Type D effect.

Ideally, the lines in each plot of these figures should be perfectly horizontal, as this would indicate that the estimated Type D effects and corresponding significance tests are independent of the size of the NA/SI main effects. Inspection of the top row of Fig. 1 shows that this was indeed the case for the continuous interaction and the adjusted 2-group approaches, both estimating the Type D effects close to the true underlying effects (i.e. the black dotted line). As the size of the NA/SI main effects became larger, these two approaches slightly underestimated only the largest Type D effects. The 2-group and 4-group approaches were both unable to correctly estimate the underlying Type D effect. When a true effect was absent, both started to

overestimate the Type D effect more as the size of the NA/SI main effects increased, suggesting that the Type D effect in these approaches is confounded by the NA/SI main effects.

In fact, the correlation between these NA/SI main effects and the estimated Type D effect was $r = 0.97$ (95%CI = 0.95, 0.99; $p < .0001$) for the 2-group approach and $r = 0.99$ (95%CI = 0.99, 1.00; $p < .0001$) for the 4-group approach, compared with $r = -0.10$ (95%CI = -0.38, 0.20; $p = .537$) for the adjusted 2-group approach and $r = -0.05$ (95%CI = -0.34, 0.25; $p = .764$) for the continuous interaction approach, indicating that the bias in the 2-group and 4-group almost perfectly followed the magnitude of the NA/SI main effects. When adjusting for these main effects, by either using the adjusted 2-group or continuous interaction approach, this correlation basically reduced to zero. These findings suggest that the 2-group and 4-group approaches do not assess a synergistic Type D effect.

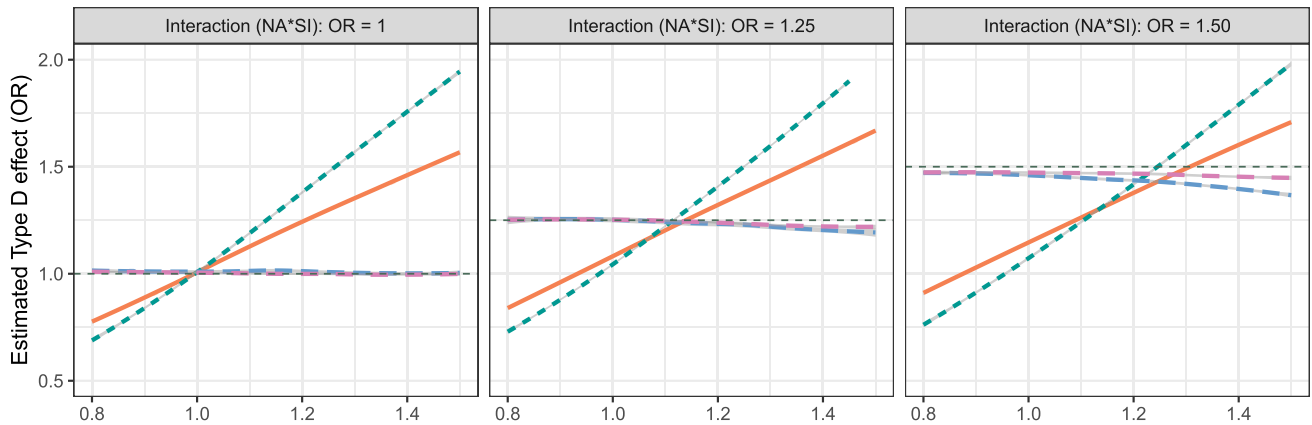
The adjusted 2-group and continuous interaction approaches show much less bias. Whether this bias was any reason for concern can be determined based on the relative bias plots in the center row of Fig. 1. The two black dotted lines mark the interval between +5% and -5% relative bias. The results of adequately performing methods should fall within this interval. It turned out that only the continuous interaction approach was unbiased based on this criterion. The adjusted 2-group approach crossed the -5% border when both the NA/SI main effects as well as their interaction effect was large.

Inspection of the percentage significant Type D effects in the bottom row of Fig. 1 indicated that both the continuous interaction and adjusted 2-group approach had an adequately controlled the false positive rate of 5% when a true effect was absent. The 2-group and 4-group approaches, however, did show adequate false positive rates when the NA/SI main effects were absent (OR = 1), but false positives increased as the NA/SI main effects became larger, up to 90% false positive findings. The middle and right columns of the bottom row show the power to detect a Type D effect when there was a true underlying effect. The 2-group and 4-group approaches showed curves similar to when the effect was absent, indicating that these approaches were not sensitive in detecting true Type D effects, but were confounded by the NA/SI main effects. With respect to the other two approaches, the continuous interaction approach consistently showed higher power to detect Type D effects than the adjusted 2-group approach, suggesting that the continuous interaction approach performed best, both in terms of minimizing bias, minimizing false positives as well as in maximizing power.

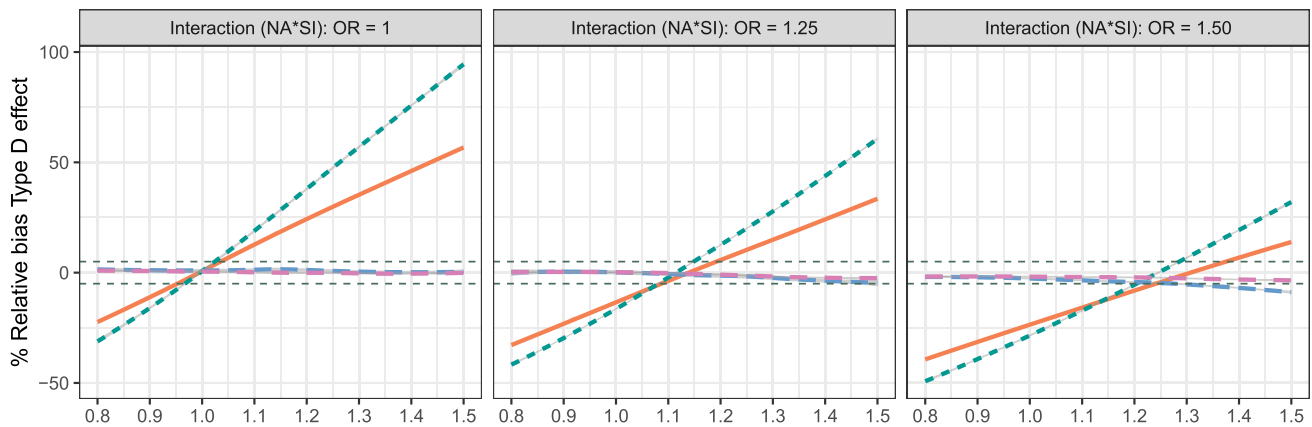
Fig. 2 shows the simulation results when one of the NA/SI traits was fixed to an odds ratio of one. For all approaches, the results were similar to our main results, though less extreme. Interestingly, the fact that the 2-group and 4-group approaches still showed bias indicates that they may falsely conclude a Type D effect even if only one of the NA/SI main effects is significant. This suggests that even if the Type D effect is not synergistic, but additive in nature, the 2-group approaches still remains biased in detecting the Type D effect, because it cannot distinguish between the following three scenarios: [1] only SI shows an effect; [2] only NA shows an effect; [3] both SI and NA show an effect.

Fig. 3 illustrates the simulation results for the 4-group approach where the Type D group was contrasted with each of the three other groups. The difference between Fig. 3 and the previous figures is that it includes an additional simulation conditions where NA and SI did not correlate, whereas in the main simulation this correlation was fixed to the value typically observed in the literature (i.e. $r = 0.5$). This correlation appeared to be important in explaining the bias in the Type D effects resulting from the 4-group approach. The leftmost column of Fig. 3 illustrates the scenario with no synergistic Type D effect, no SI effect and no correlation between NA and SI. The results indicated that as the size of the NA effect increased, the contrasts between the Type D group and both the reference group (NA- SI-) and the High SI group (NA- SI+) also increased, while the contrast with the High NA group (NA+ SI-) remained zero on average, with an expected false positive

Average estimated odds ratio of the Type D effect



Percentage relative bias in estimated Type D effect



Percentage significant Type D effects

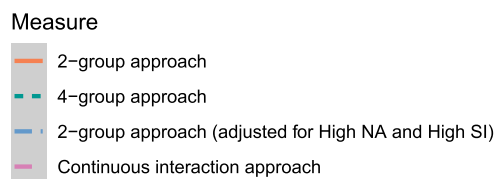
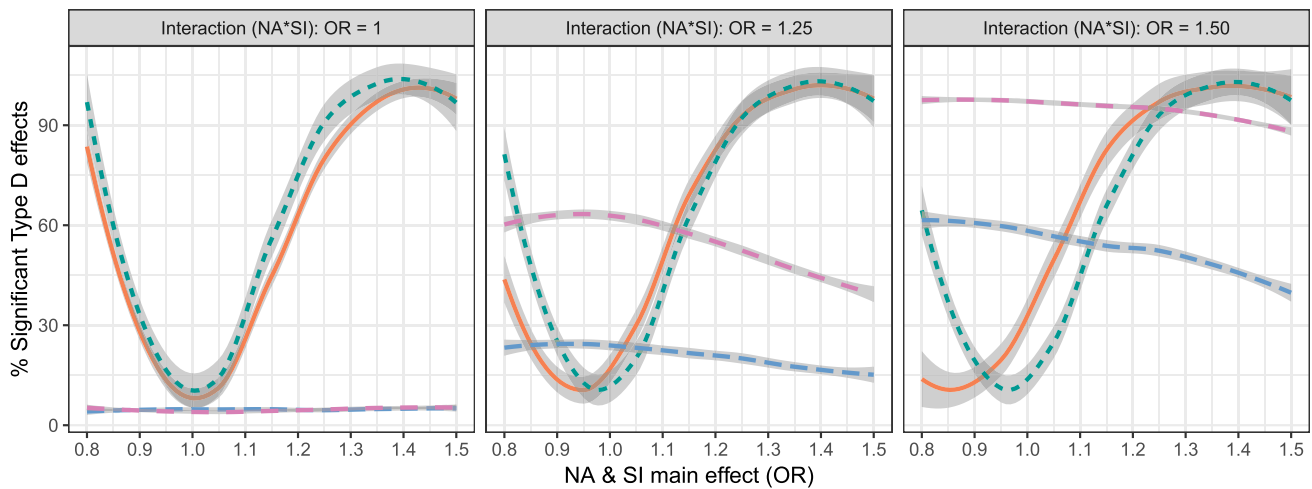
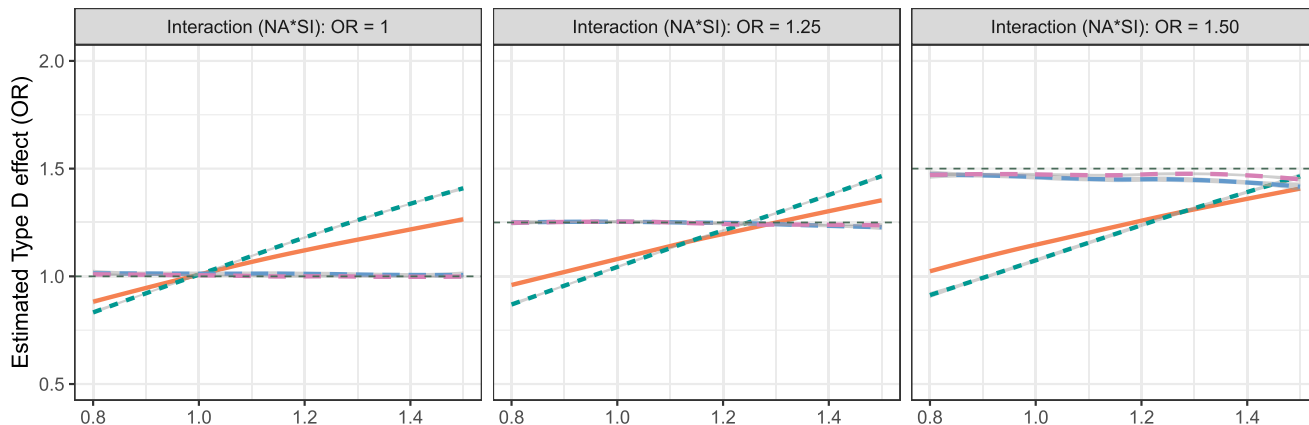
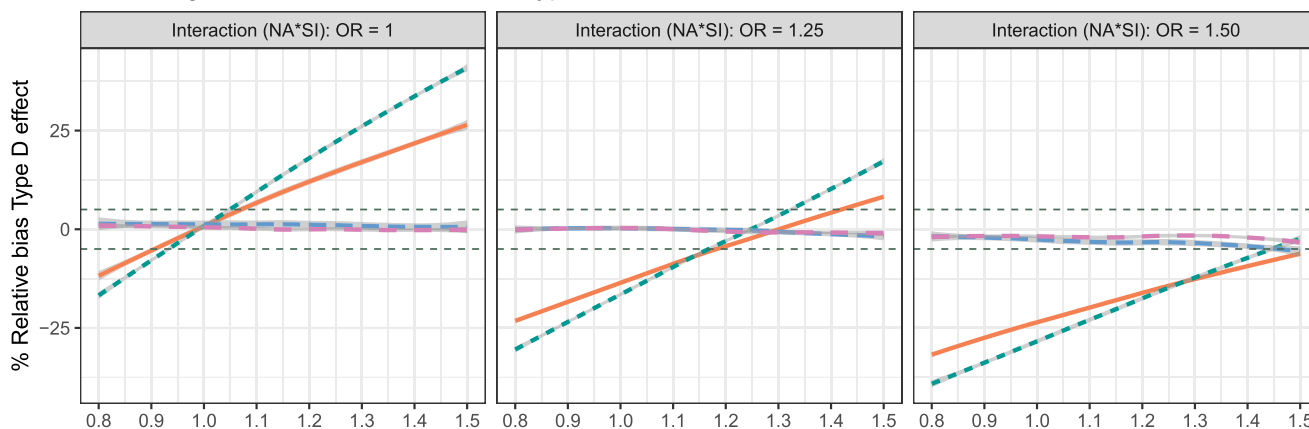


Fig. 1. For each Type D operationalization and for varying levels of the Type D effect and the NA and SI main effects, the mean estimated odds ratio (upper), percentage relative bias (middle) and percentage significant results (lower) of the Type D effect.

Average estimated odds ratio of the Type D effect



Percentage relative bias in estimated Type D effect



Percentage significant Type D effects

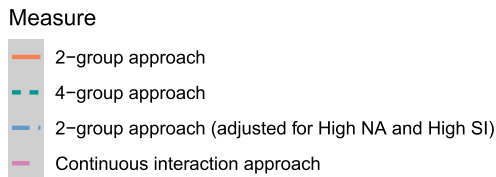
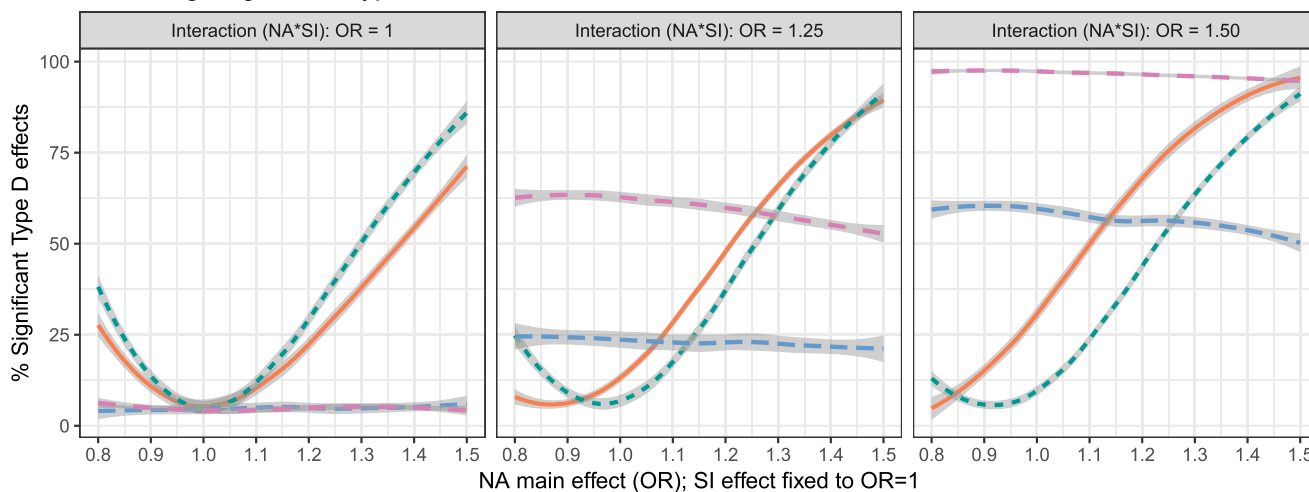


Fig. 2. For each Type D operationalization and for varying levels of the Type D effect and the NA main effect on a dichotomous outcome (SI main effect is fixed at OR = 1), the mean estimated standardized regression coefficient (upper), percentage relative bias (middle) and percentage significant results (lower) of the Type D effect.

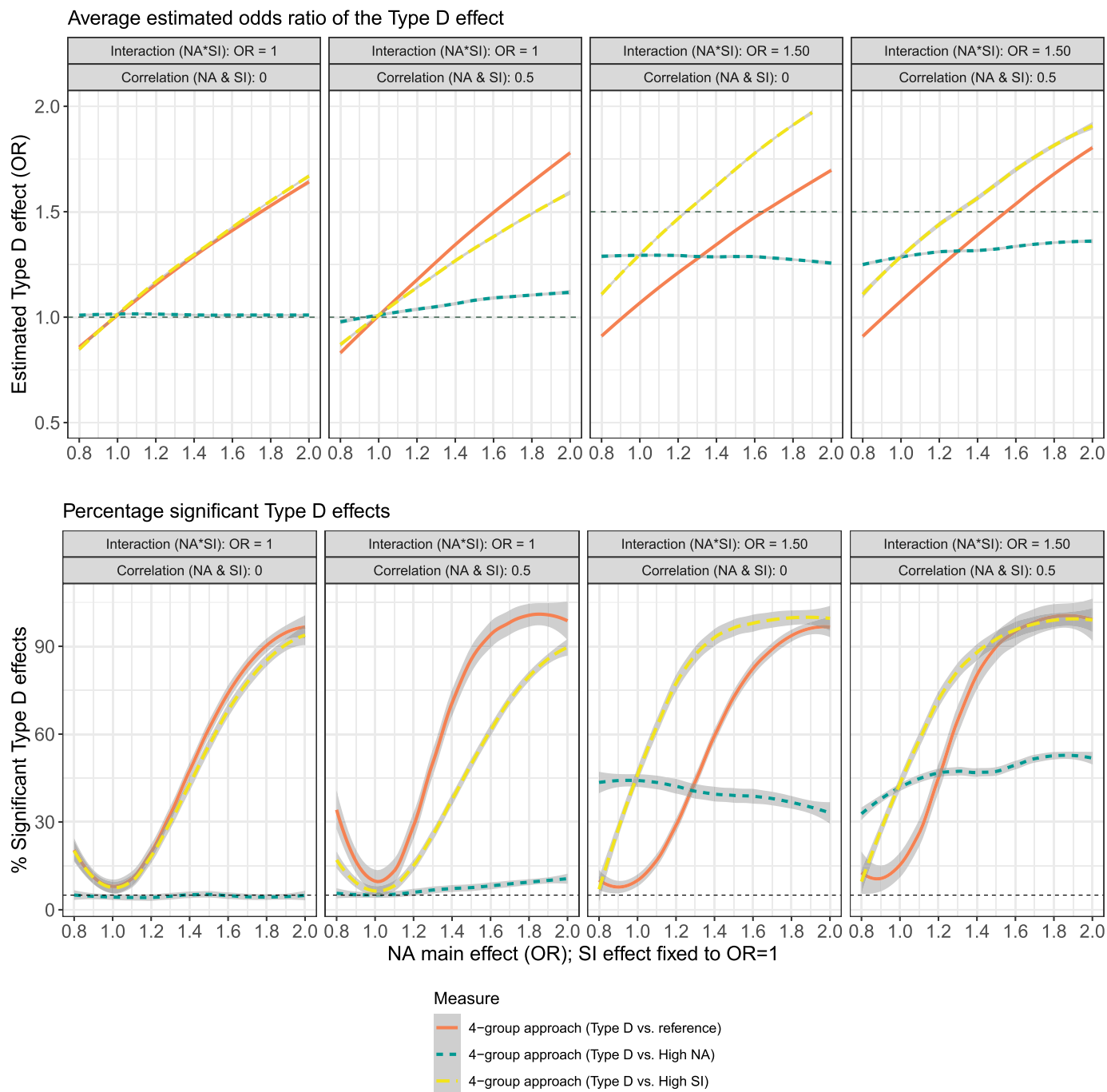


Fig. 3. For varying levels of the synergistic Type D effect and NA main effect on a dichotomous outcome (SI main effect is fixed at OR = 1), the mean estimated standardized regression coefficient (upper) and percentage significant results (lower) of the Type D effects estimated by the 4-group approach.

rate similar to the chosen significance level of 5%. In this condition the 4-group method performed as expected, because when only NA is related to the outcome, the two group containing elevated NA scores (the Type D & High NA groups) should differ significantly from the two groups with low NA scores (the reference group and High SI group), but not from each other.

The second column of Fig. 3 shows the results when increasing the correlation between NA and SI to 0.5. This change resulted in overestimated Type D effects relative to both the reference and high NA groups, and this bias got stronger as the size of the NA main effect increased. This is not desirable, because when only NA is related to the outcome, people in the Type D group should not differ from people in

the High NA group. It also turned out that the effect of the Type D group relative to the reference group became larger than the effect of the Type D group relative to the High SI group. This is also not desirable, because the reference and High SI groups should show equal effects when only NA is related to the outcome.

The explanation for these biased results is that the positive correlation between NA and SI causes some of the NA effect to spill over to SI, resulting in overestimated effects for the groups with elevated SI scores (the Type D group and High SI group). In continuous analyses this does not happen because there the effect of SI is adjusted for the effect of NA. However, this adjustment is no longer adequately performed when artificially categorizing two correlated continuous

variables in 4 separate groups.

3.2. Sensitivity analyses

Three supplemental figures show the simulation results for several sensitivity analyses, to show that are results are not contingent on specific design choices in our simulation. Supplementary Fig. 1 shows the simulation results for less than additive interaction effects. Although Type D theory predicts the interaction between NA and SI to be more than additive, the inclusion of this sensitivity analysis may improve the generalizability of our results to fields where less than additive interactions are of interest. The results in Fig. S1 are similar to those in Fig. 1: The Type D effects estimated by the 2-group and 4-group varied with the size of the NA and SI main effects, while the Type D effect estimated with the continuous interaction method and adjusted 2-group approach did not. The 2-group and 4-group approaches showed high false-positive rates when a synergistic Type D effect was absent and the NA or SI main effects were present. Although the false-positive rates of both the continuous interaction method and adjusted 2-group approach were adequate, the continuous method outperformed the adjusted 2-group method in terms of power to detect the Type D effect.

Supplementary Fig. 2 shows the simulation results for continuous outcomes. These results are largely similar to those found for dichotomous outcomes. Both the 2-group and 4-group approaches failed to detect the Type D effect and merely picked up the presence of NA/SI main effects. The adjusted 2-group and continuous interaction approaches both showed much less biased, yet they slightly underestimated the true Type D effect as the size of the NA/SI main effect increased. The 2-group and 4-group approaches showed very high false positive rates. The power to detect true Type D effects was best for the continuous interaction approach.

Supplementary Fig. 3 shows the simulation results of the sensitivity analysis where the ordinal NA/SI item scores were positively skewed rather than normally distributed. The results were largely similar to normally distributed item scores. However, all methods showed attenuated estimates of the Type D effects as the NA/SI main effects became larger. For the 2-group and 4-group approaches this attenuated the earlier found positive bias, while for the adjusted 2-group and continuous interaction approaches it resulted in somewhat underestimated Type D effects. As a result, the power of these approaches to detect true Type D effect decreased as the NA/SI main effects became larger. Thus, large main effects for skewed variables obfuscated the presence of true interaction effects.

3.3. Empirical reanalysis

In order to validate the results of our simulation study we have reanalyzed earlier published data of two empirical studies investigating the association between Type D personality and various dichotomous outcomes. If the results of our simulation are accurate, one would expect to find similar patterns when analyzing empirical data using the four operationalizations of Type D personality. For each of the two datasets and for each of the four operationalizations we have reported the odds ratios of the Type D effect in Table 2. To allow for comparison across operationalization methods, we have calculated the odds ratios based on the standardized logistic regression coefficients.

Using the first dataset [36], we reanalyzed the association between Type D and elevated depressive symptoms in a sample of 650 outpatients with chronic heart failure. In the second dataset [13] we reanalyzed the association between Type D personality and endothelial dysfunction in a sample of 180 patients with coronary artery disease. Reanalysis of these two datasets showed results strikingly similar to the patterns found in our simulation study. First, for each dataset the 2-group and 4-group approach showed statistically significant effects, while the adjusted 2-group and the continuous interaction approach did not. Second, in both datasets the 4-group approach resulted in larger

Table 2

Study characteristics of two different datasets investigating Type D personality, and the estimated odds ratio (95% CI) of the Type D effect, according to four operationalizations of Type D personality.

Dataset	Pelle et al. [36]	Denollet et al. [13]
<i>Study characteristics</i>		
Sample size	641	180
Outcome	Elevated depression	Endothelial dysfunction
NA main effect	2.18 (1.92, 2.48)	1.10 (0.80, 1.49)
SI main effect	1.01 (0.92, 1.11)	1.46 (1.06, 2.02)
<i>Type D operationalization</i>		
2 groups	1.49 (1.38, 1.62)	1.41 (1.04, 1.90)
4 groups	1.75 (1.58, 1.94)	1.60 (1.11, 2.33)
2 groups (adjusted for NA + & SI +)	0.99 (0.86, 1.15)	1.07 (0.79, 1.44)
Continuous interaction (NA * SI)	1.00 (0.99, 1.01)	1.05 (0.79, 1.41)

Note: all Type D effects are odds ratios (95%CI) based on the standardized regression coefficients of the Type D effect. Bold faced results indicate a statistically significant odds ratio with a *p*-value smaller than 0.05.

CAD = coronary artery disease; NA = negative affectivity sum score; NA+ = NA score above cutoff (yes/no); SI = social inhibition sum score; SI+ = SI score above cutoff (yes/no).

odds ratios than the 2-group approach, similar to our simulation results. Interestingly, in both datasets only one of the NA/SI main effects was significant. Similar to the results of our simulation study, the reanalysis suggests that the 2-group and 4-group approaches do not detect synergy, and that they also do not detect the combined presence of the NA and SI main effects, because only one of the main effects has to be present before these approaches result in a significant Type D effect.

4. Discussion

In this study we showed that the most commonly used operationalizations of Type D personality failed to detect the presence of a synergistic Type D effect. These results apply to models with either a dichotomous or a continuous observed outcome. When a true synergistic effect was absent, the chance that the 2-group and 4-group approaches found significant effect increased at an alarming rate as the size of the NA/SI main effects became larger. Our simulations showed this problem to occur even when only one of the NA/SI main effects was present and the other absent. Regardless of whether the Type D effect is synergistic or additive in nature, the most commonly used 2-group approach did not assess how NA and SI interact or combine; it was merely sensitive to the presence of *any* main effect. Interestingly, the 2-group and 4-group approaches showed an almost perfect correlation between their estimated Type D effects and the true size of the NA/SI main effects. These findings support Smith's [2] hypothesis that the 2-group approach may falsely conclude the presence of a Type D effect when only NA/SI main effects are present.

The continuous interaction and adjusted 2-group approaches were both relatively unbiased and showed acceptable false positive rates. However, the statistical power to find a Type D effect based on the adjusted 2-group approach was only 50 to 70% the size of the power to detect such effects using the continuous interaction approach. As noted by Smith [2], this might have been caused by the fact that the 2-group approach uses dichotomized predictors. Indeed, earlier research has indicated that dichotomization of continuous predictors may decrease precision to 65% of when using continuous predictors [37].

Regarding the 4-group approach, our study showed that not only the contrast between the Type D group and reference group was biased, but also the contrast between the Type D groups and the other contrasts. These results imply that when only NA is related to an outcome, the 4-group approach not only results in significant Type D effects relative to the reference group and high SI group, but also results in false positive Type D effects relative to the High NA group, falsely suggesting the

presence of a synergistic Type D effect. When only one of two traits is related to an outcome, the positive correlation between the traits causes elevated scores for people scoring high on the other trait, and this bias increases with the size of the correlation. This suggests that two correlated continuous variables should never be categorized in groups based on the different combinations of scoring high or low on these variables. This recommendation does not only apply to research on Type D personality, but to any field where two correlated continuous variables are categorized in subgroups.

The patterns found in our simulation study were corroborated in our reanalysis of empirical studies on Type D personality. For all analyses, the continuous interaction approach failed to reach significance, with odds ratios close to one, while the 2-group and 4-group approaches showed a significant Type D effect with odds ratios varying between 1.2 and 1.6. In light of the results of our simulation one would expect this pattern in a scenario where NA and/or SI have positive main effects, yet no synergy. Each reanalysis suggested that not Type D personality, but merely one of its subcomponents was related to the outcome. Although these reanalyses seem to suggest there is no synergistic Type D effect underlying these empirical studies, we cannot exclude the possibility of a true but small synergistic effect that could not be detected due to low statistical power.

This highlights the importance of reanalyzing other published research on Type D personality using the 2-group and 4-group approaches. Echoing earlier recommendations [2,21], we therefore encourage the authors of those publications to reanalyze their data using the continuous interaction approach. Future meta-analyses on Type D personality should use individual patient data rather than aggregated study level data, to allow for assessing the overall Type D effect according to the continuous interaction approach. Future clinical studies on Type D personality should be sufficiently powered to detect the Type D effect according to the continuous interaction approach. More importantly, we recommend against using either the 2-group or 4-group approach in future studies on Type D personality. Under the assumption that the Type D effect is synergistic, we advise researchers to always use the continuous interaction approach, as it outperformed all other approaches in terms of minimizing bias, minimizing false positives and maximizing power. Although the adjusted 2-group approach performed comparably in terms of bias, it showed lower power to detect true effects. Furthermore, a recent simulation study showed that including two dichotomized predictors in a regression analysis may result in spurious interaction effects [25], suggesting that continuous variables should always be assessed on their original scale. In line with suggestions by Smith [2], a re-analysis of published studies using the correctly specified continuous interaction approach may clarify whether the significant Type D effects reported in the literature are really a synergistic interaction between NA and SI, or an additive combination of NA and SI, or a main effect of NA or SI only.

4.1. Counter arguments

We will now discuss several arguments that could be raised against our conclusions. First, typical bar plots resulting from the 4-group method (see for instance Fig. 4) may suggest that the Type D group does in fact show higher mean scores or percentages than the other three personality subgroups. If the Type D effect according to the 4-group approach is biased, why do the results in Fig. 3 seem to suggest that people with a Type D personality less often have a romantic partner? We argue that bar plots such as Fig. 3 may be misleading because they are unable to visualize the presence of synergistic effects. Let's assume that both NA and SI show a main effect on having no romantic partner. Let's further assume there is no synergistic effect between NA and SI. Such an additive model can perfectly explain the differences between the personality groups visualized in Fig. 3. If both NA and SI show a main effect, then people who score high on both NA and SI already have a higher chance on living without a partner, than people who score high

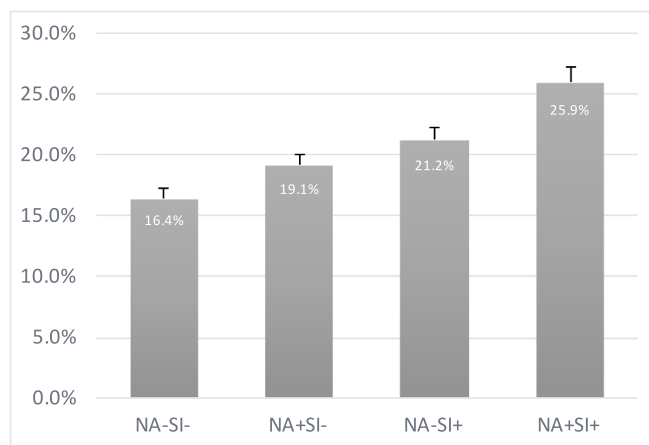


Fig. 4. Example of a bar plot resulting from the 4-group approach, showing for each of the four personality subgroups the percentage of participants having a romantic partner. Underlying this simulated data are main effects for both NA and SI, but no synergistic effect.

on only one of those traits. That is, when predicting an individual outcome using the regression equation, the individual contributions of the NA and SI effects are already combined due to their additive nature. For this reason, though Fig. 3 may suggest the presence of synergy, such bar plots are in fact not able to visualize the difference between synergistic models and models containing main effects only.

Second, one could argue that the Type D effect is not synergistic and merely describes the additive influence of the NA and SI main effects. Our findings indicate that the 2-group and 4-group approaches are to a large extent capturing the additive influence of the NA and SI main effects, rather than their interaction. However, these methods are not even adequate in detecting additive NA and SI effects for three reasons: [1] our stimulation showed that these approaches have difficulty in concluding whether the effect is caused by NA only, or by SI only, or by both NA and SI; [2] using dichotomized variables in regression analyses results in lower power to detect significant effects [20,22]; [3] using dichotomized variables in regression analyses risks spurious main effects and interactions, especially when the two variables are correlated [25,26] or when measurement error in the item scores is not taken into account [22].

Are there reasons to assume that the Type D effect is synergistic? As noted in our introduction, earlier writings on Type D personality do suggest that the Type D effect is *more* than additive [4–8]. Moreover, the most commonly used Type D vs. non Type D operationalization is itself a type of interaction variable, as this two group dichotomy is statistically equivalent to a multiplication of the dichotomized NA and SI variables. Taken together this would suggest that the Type D effect is synergistic rather than additive. However, if researchers would on second thought conclude that the Type D effect is better seen as additive than synergistic, then this would require all further analyses to restrict their focus on the additive NA/SI effects. These main effects should then be entered as *continuous* variables in regression analyses, because using their dichotomized versions (i.e. the 2-group and 4-group approach) will not only result in lower power, but also risks both spurious main [23] and interaction effects [25]. Note that such an additive model does not necessarily have to be a linear model. Non-linear models such as quadratic, spline, or threshold regression models are perhaps more suitable in testing the additive continuous NA and SI effects, while taking into account the idea that these traits are only influential above a cut-off score of 10 [18].

Another counterargument against our findings could be that we assumed the data generating mechanism in our simulation study to be variable centered rather than person centered [38,39]. Variable centered approaches investigate the association between two or more

dimensions (variables) within a population. In contrast, person centered approaches aim at classifying individuals in distinct subgroups or classes of people with similar characteristics. Regression models (e.g. linear regression; logistic regression; structural equation modeling) are an example of variable centered analyses, while clustering methods (e.g. cluster analysis; latent class analysis) are examples of person centered approaches. Those two approaches are not mutually exclusive and some have even argued that the difference between them is itself a matter of degree [40]. One could argue that the validity of our simulation results would be threatened if the assumed data generating mechanism differs from the true data generating mechanism. It could be that the true mechanism underlying the Type D effect is person centered, with a set of distinct latent personality classes giving rise to the different score patterns on the DS14 questionnaire. However, some have argued that a person centered approach is not appropriate when modeling Type D as there are reasons to doubt it is a *categorical* latent construct. First, though we agree that a mismatch between the true and assumed data generating mechanism could potentially invalidate the findings of our simulation study, it still remains to be explained why the findings of our empirical reanalysis show exactly the same pattern as expected when the results of our simulation study are valid. Second, the individual difference literature suggest that personality traits are dimensional [15,16]. Third, the personality type variables are *constructed* to be categorical by reducing the scores on two or more personality traits to a limited number of personality types. Subsequently concluding without empirical evidence that these typologies have concrete existence (i.e. reification) would be committing the fallacy of misplaced concreteness [41]. Moreover, while the existence of personality types would imply a bimodal NA and SI distribution, the empirical results indicate these constructs show unimodal distributions [17]. Hence, the burden of proof is on those claiming that Type D personality is a categorical latent construct. But even when its categorical nature would be empirically supported, we would argue for analyzing these personality types as continuous variables. Categorizing continuous traits may result in heterogeneous groups of people as most would not fit the prototypical personality type. Modeling the personality types as continuous scores in statistical analyses, by expressing them as the person's similarity to the prototypical personality type, would more accurately capture such heterogeneity [42].

A limitation of our simulation study is that we merely focused on an interaction between the NA and SI main effects, thereby excluding other nonlinear (e.g. quadratic, cubic, spline) effects and their Interactions. Future research could build upon our work by studying how the various Type D operationalizations perform in detecting such nonlinear NA and SI effects and the interactions between them.

A limitation of our empirical study is that we only reanalyzed two datasets. This is only a small part of the numerous studies that have investigated the association between Type D personality and a wide range of medical and psychosocial outcomes. Future research could therefore focus on replicating our findings by comparing the results of the four Type D operationalizations in as many datasets as possible.

5. Conclusion

This study showed that synergistic effects can best be modeled using a continuous interaction approach. Other approaches showed either more bias, more false positive findings or lower power. We showed that the most commonly used operationalizations of Type D personality result in false positive Type D effects when only an NA or SI effect is present. Reanalysis of several Type D studies showed that the significant effects according to these commonly used methods were no longer significant when using the correct continuous interaction approach. However, there still remain plenty of studies showing significant Type D effects using the continuous interaction approach [8,17,43–45]. Regardless of whether the Type D effect is synergistic or additive, our results imply that findings of earlier research on Type D

personality should be reconsidered if they were based on dichotomized subgroup approaches. The present study served as a first step in separating the wheat from the chaff.

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Appendix A. Supplementary data

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