

Type D personality as a risk factor for adverse outcome in patients with cardiovascular disease

An individual patient data meta-analysis



CoRPS

No conflicts of interest or funding to report

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AIM

SHOW THAT TYPE D PERSONALITY IS A
RISK FACTOR FOR ADVERSE EVENTS IN
CORONARY ARTERY DISEASE PATIENTS





Overview

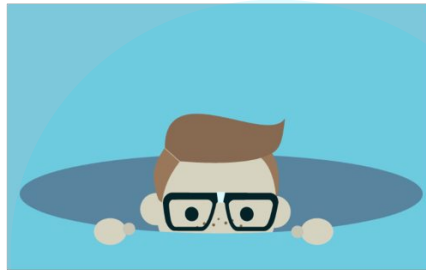
1. Type D personality
2. How to estimate Type D effects?
3. Individual patient data meta-analysis
4. Limitations and future research
5. Conclusion

1

Type D personality

- High scores on **two** personality traits:
 - Negative affectivity (NA)
 - Social inhibition (SI)
- The **DS14** questionnaire measures NA and SI
 - 14 items on 0-4 Likert scale
 - Example (NA): I often take a gloomy view of things
 - Example (SI): I would rather keep other people at a distance

Negative affectivity & Social inhibition



1

Type D personality

- Related to various medical and psychosocial outcomes
- Risk factor for adverse events in cardiovascular disease
 - Early studies showed large effects
 - More recent work did not replicate some findings
 - [Meta-analysis](#): Type D as risk factor in CAD, but not CHF (Grande et al., 2012)
 - Moderating role of age and type of endpoint (Kupper & Denollet, 2018)
 - The importance of the Type D operationalization (Smith, 2011)

Grande, G., Romppel, M., & Barth, J. (2012). Association between type D personality and prognosis in patients with cardiovascular diseases: a systematic review and meta-analysis. *Annals of behavioral medicine*, 43(3)

Kupper, N., & Denollet, J. (2016). Explaining heterogeneity in the predictive value of Type D personality for cardiac events and mortality. *International journal of cardiology*, 224.

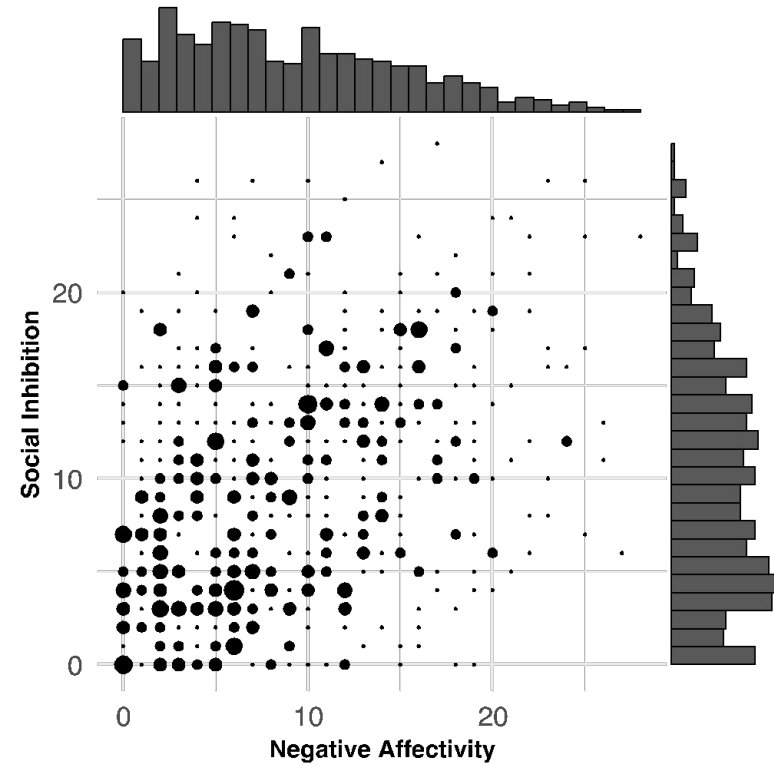
Smith, T. W. (2011). Toward a more systematic, cumulative, and applicable science of personality and health: lessons from type D personality. *Psychosomatic medicine*, 73(7)



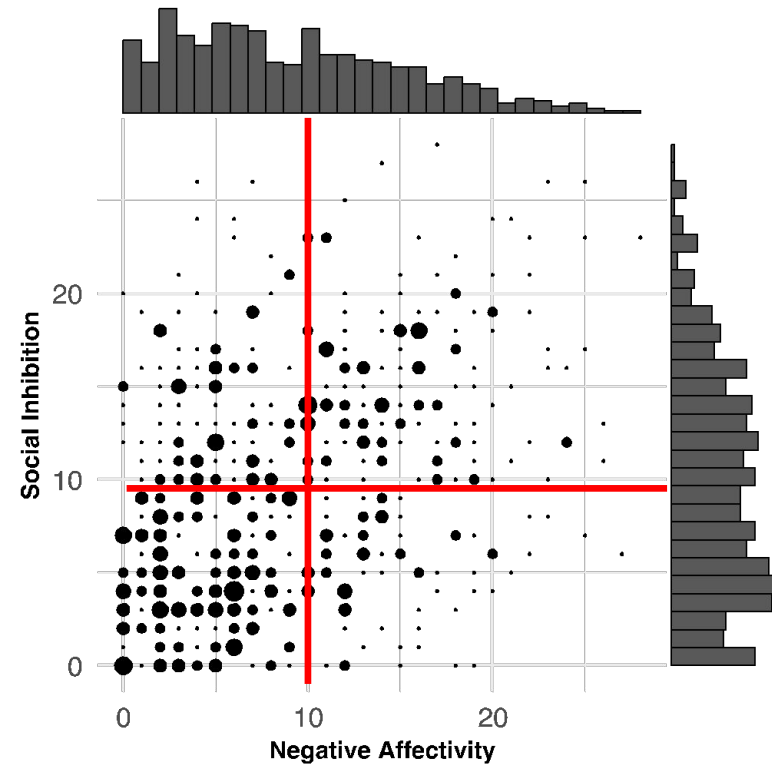
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How to estimate Type D effects?

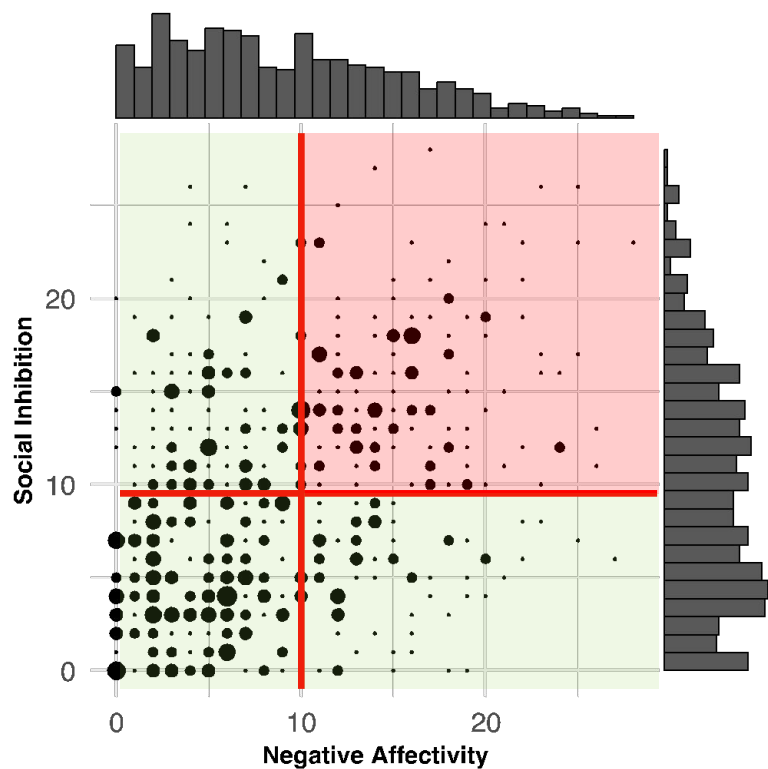
Example data: NA & SI sum scores



Cut-off score: 10 or higher



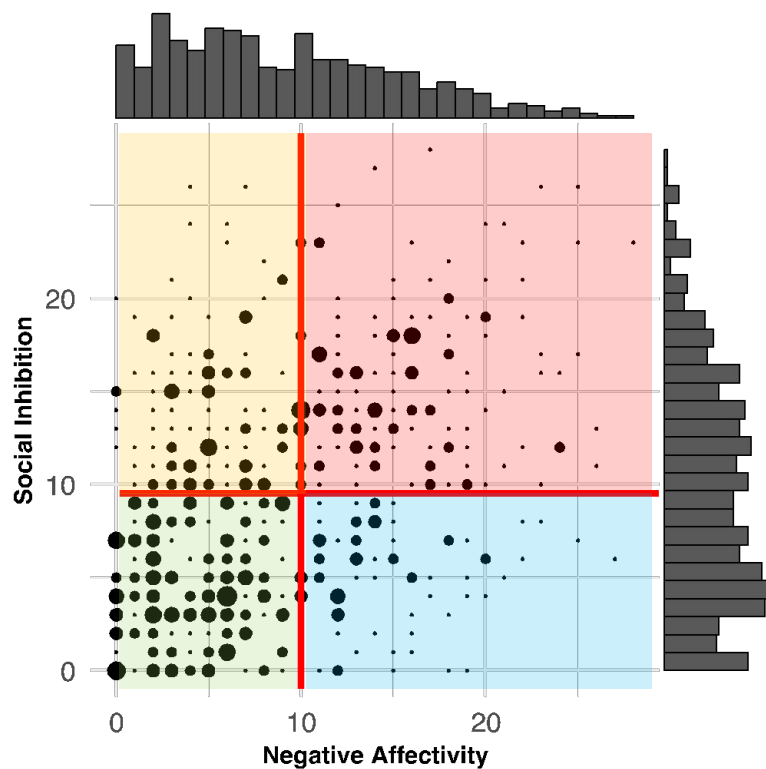
2-group method



Type D
No Type D

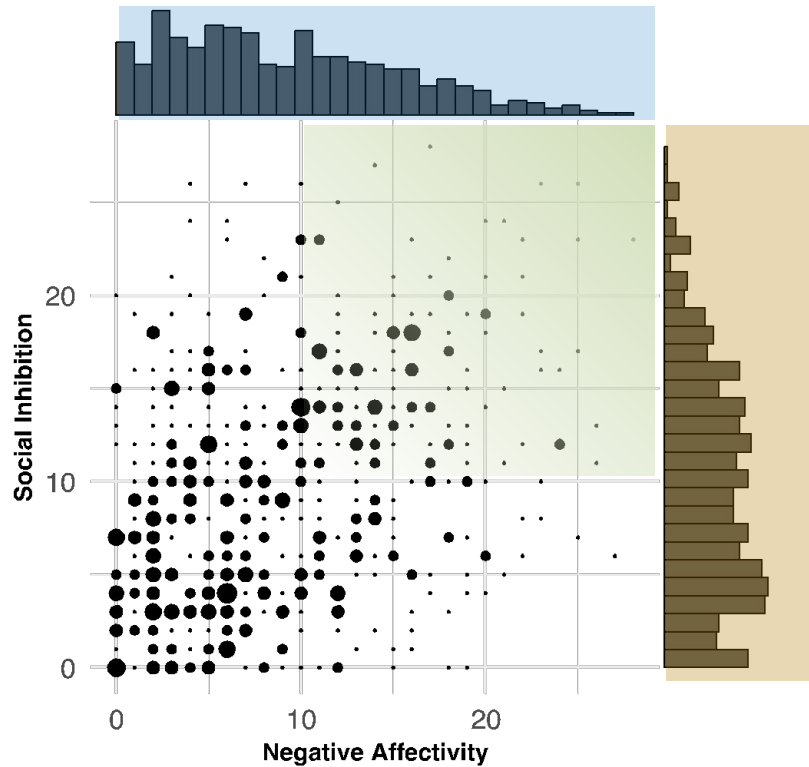


4-group method



Type D
NA- SI-
NA- SI+ } No Type D
NA+ SI-

Continuous method




- SI
- NA
- NA * SI (Type D)

Data simulation studies

False positive Type D effects for 2-group & 4-group methods:

- **If** only NA **or** SI was related to an outcome
- **Then** these methods often indicated Type D effects
- Continuous method did not show this bias




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
Journal of Psychosomatic Research

journal homepage: www.elsevier.com/locate/jpsychores



Modeling synergy: How to assess a Type D personality effect


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Does this bias affect the Type D literature?



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General Hospital Psychiatry

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Review article

A systematic review comparing two popular methods to assess a Type D personality effect

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^b Center of Research on Psychology in Somatic diseases (CoRPS), Department of Medical and Clinical Psychology, Tilburg University, the Netherlands




Of all reviewed studies with a significant 2-group Type D effect:

- 37% showed a Type D effect based on continuous method
- 63% did not show a Type D effect!
- 48% merely showed an effect of NA or SI

Even the continuous method can be biased!

False positive Type D effects for continuous methods:

- **If** only NA **or** SI is quadratically related to an outcome
- **And if** the quadratic effects are not modeled
- **Then** false positive NA*SI interactions can occur



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Personality and Individual Differences

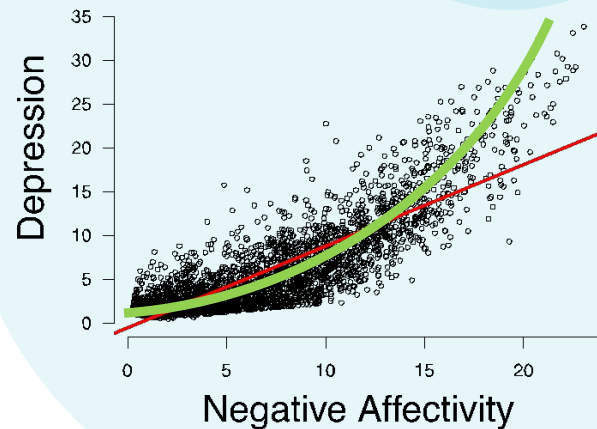
journal homepage: www.elsevier.com/locate/paid

A re-evaluation of the Type D personality effect

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Reconsidering the Type D literature

- Observation 1: Major discrepancy in conclusions 2-group vs continuous method
- Observation 2: Most published studies used the 2-group method
- Observation 3: Earlier meta-analyses were based on the on 2-group method
- Problem? These studies cannot distinguish Type D from NA or SI effects
- Solution? Re-analysis of earlier literature with continuous method
- How? Individual patient data meta-analysis





3

Individual patient data meta-analysis

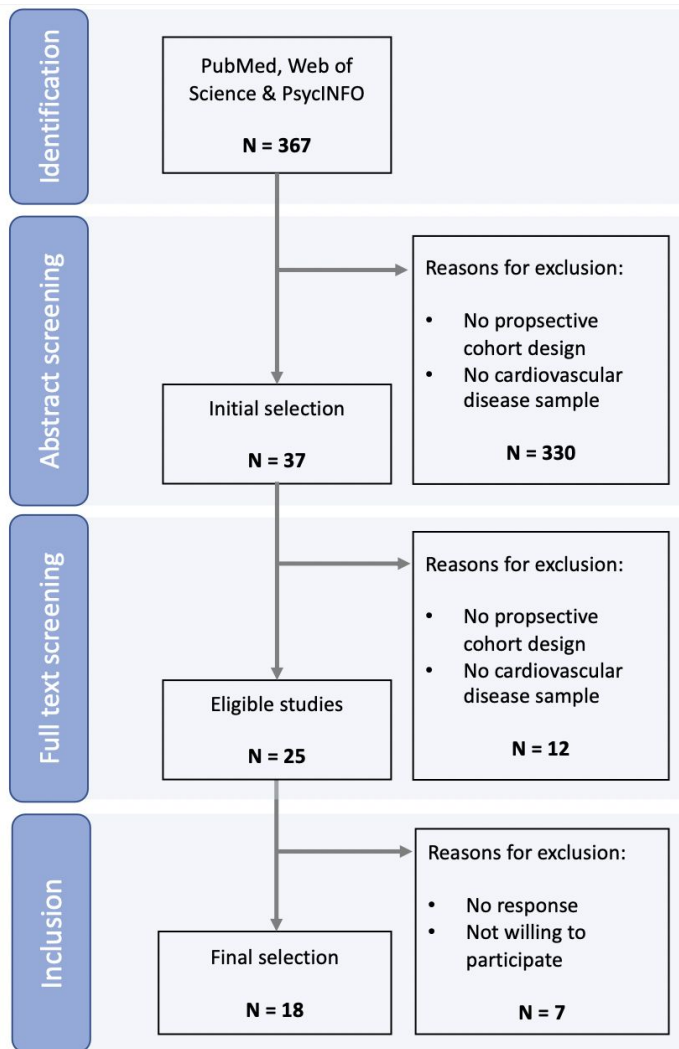
Inclusion criteria

- Prospective cohort studies (1995-2020)
- Cardiovascular disease patient populations:
 - Coronary artery disease
 - Heart failure
 - Ventricular arrhythmia
- Self report measurements of NA and SI
- At least one type of adverse event recorded during follow-up
 - All-cause mortality
 - Cardiac mortality
 - Myocardial infarction
 - Coronary artery bypass grafting (CABG)
 - Percutaneous coronary intervention (PCI)

MACE

Any adverse event

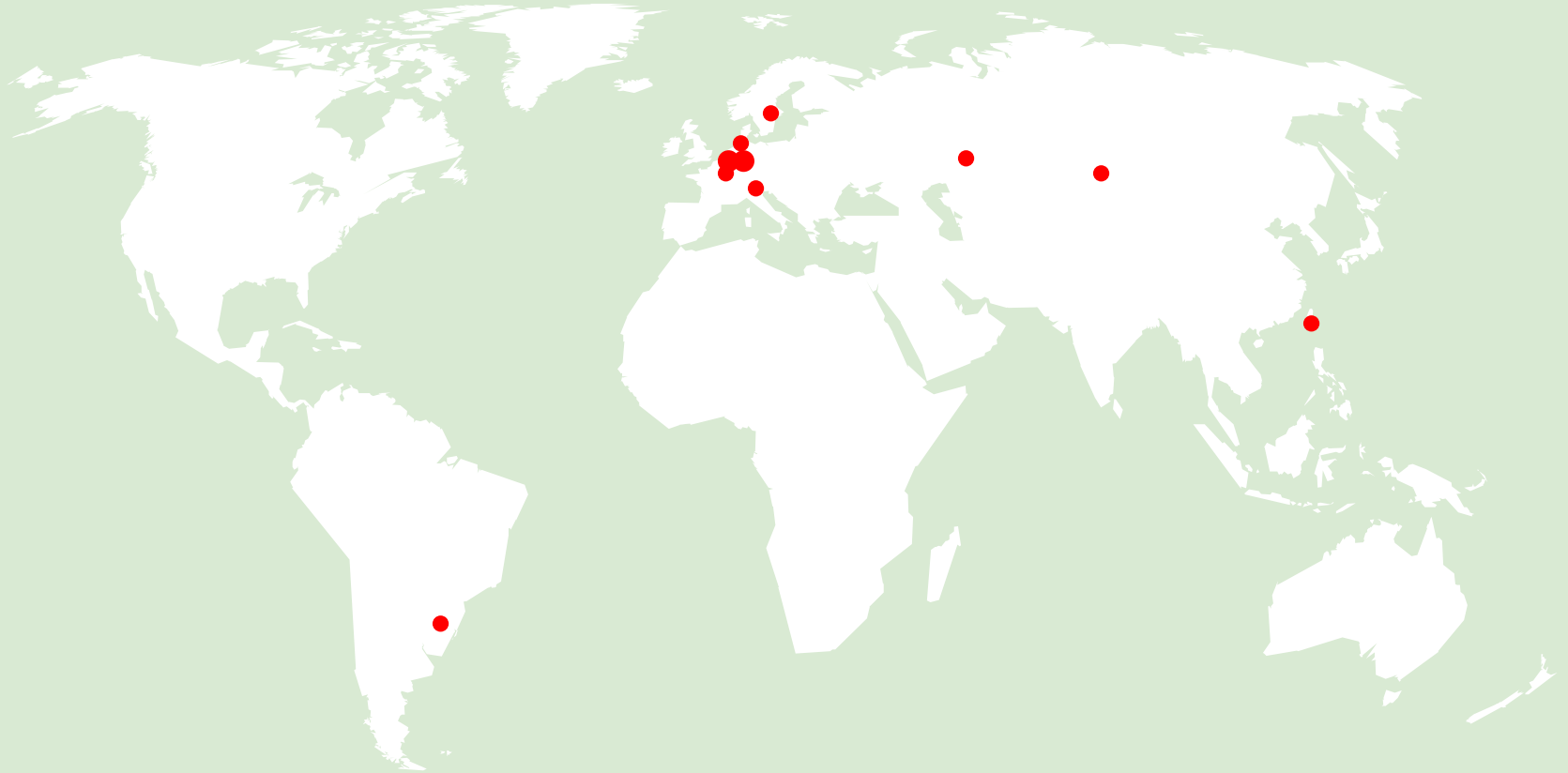
Flowchart



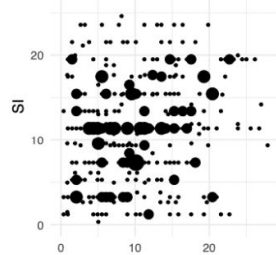
Study characteristics

Study	Journal	N	Diagnosis	Follow-up (months)	Age (M)	Males (%)
Denollet et al. (1996)	The Lancet	378	CAD	95	55.6	88.60%
Denollet et al. (2000)	Circulation	364	CAD	60	56.5	91.80%
Pedersen et al. (2010)	Europace	326	VA	20	56.8	87.10%
Martens et al. (2010)	The Journal of Clinical Psychiatry	466	CAD	22	59.3	78.50%
Pelle et al. (2010)	Circulation. Heart failure	641	HF	37	66.4	74.30%
Schmidt et al. (2011)	Arquivos Brasileiros de Cardiologia	137	CAD	12	60.2	63.50%
Coyne et al. (2011)	Psychosomatic medicine	1047	HF	18	70.9	62.60%
Albus et al. (2011)	Journal of Psychosomatic Research	569	CAD	18	59.2	78.90%
Grande et al. (2011)	Psychosomatic Medicine	1091	MIX	71	62.7	74.80%
Denollet et al. (2013a)	International journal of cardiology	638	VA	38	62.9	80.60%
Denollet et al. (2013b)	Psychosomatic medicine	541	CAD	60	58.7	87.40%
Meyer et al. (2014)	Annals of behavioral medicine	470	CAD	60	63.7	76.80%
Sumin et al. (2015)	Kardiologiya	682	CAD	12	58.5	81.80%
Dulfer et al. (2015)	Journal of Psychosomatic Research	1190	CAD	120	62.3	72.60%
Gostoli et al. (2016)	International journal of cardiology	117	VA	24	63.1	74.40%
Pushkarev et al. (2017)	Kardiologiya	939	CAD	12	58.7	75.30%
Conden et al. (2017)	European journal of preventive cardiology	941	CAD	76	70.5	66.70%
Lin et al. (2019)	PLOS ONE	222	HF	18	60.4	66.20%
Overall		10759		47	62.6	75.8%

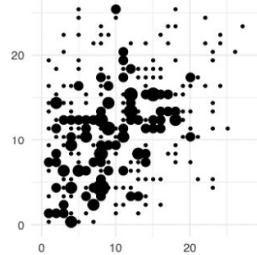
Location of included studies



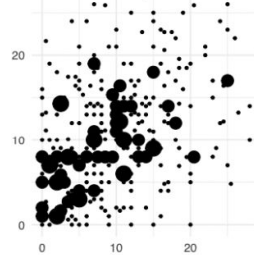
Denollet et al. (1996)



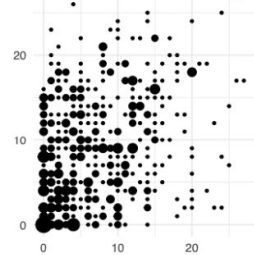
Denollet et al. (2000)



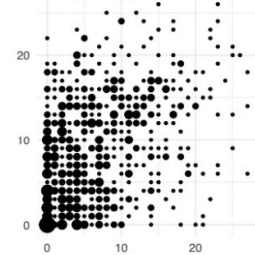
Pedersen et al. (2010)



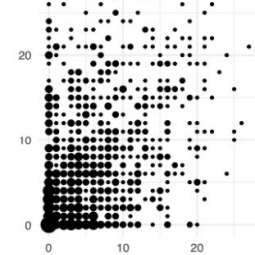
Martens et al. (2010)



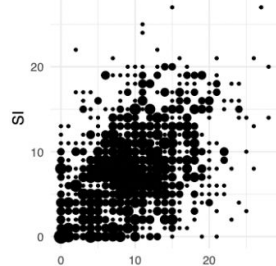
Pelle et al. (2010)



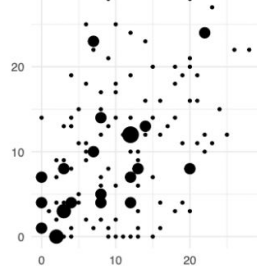
Coyne et al. (2011)



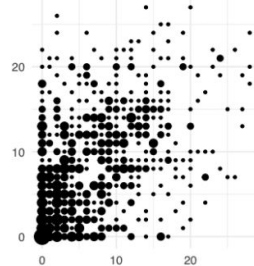
Grande et al. (2011)



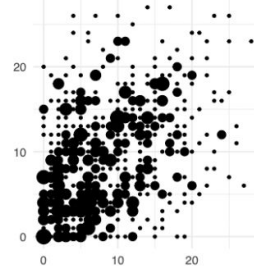
Schmidt et al. (2011)



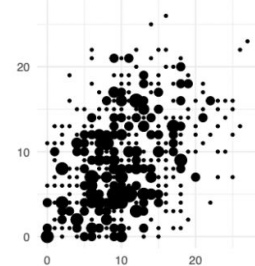
Denollet et al. (2013a)



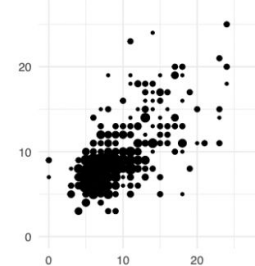
Denollet et al. (2013b)



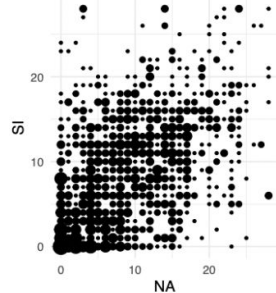
Meyer et al. (2014)



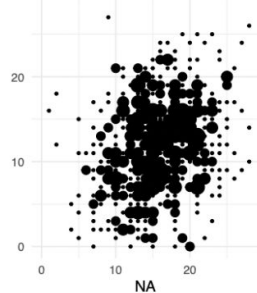
Sumin et al. (2015)



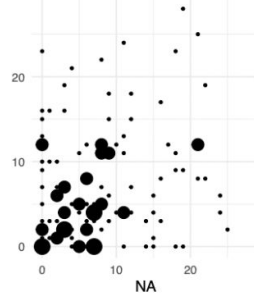
Dulfer et al. (2015)



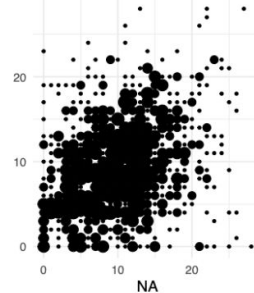
Albus et al. (2016)



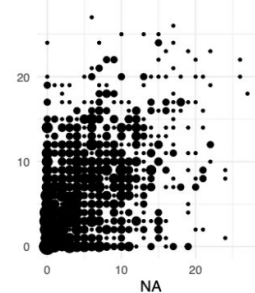
Gostoli et al. (2016)



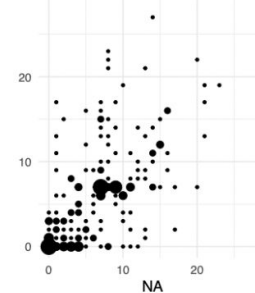
Pushkarev et al. (2017)



Conden et al. (2017)



Lin et al. (2019)



NA

SI

Statistical analysis

- Bayesian multilevel multivariable logistic regression
 - **Bayesian**: bayes factors express evidence in favor of null/alternative hypothesis
 - **Multilevel**: separating between/within-study variance
 - **Multivariable**: all continuous Type D effects adjusted for age and sex
 - **Logistic regression**: no time to-event data available
- Additional analyses
 - Do age and sex moderate the Type D effect?
 - Separate models for CAD or HF patients only



Odds ratio estimates

Outcome	All-cause mortality	Cardiac mortality	Myocardial infarction	CABG	PCI	MACE	Any adverse event
Sample size	N = 10255	N = 5774	N = 5877	N = 2440	N = 2448	N = 3923	N = 3935
Predictor	OR [95%CI]	OR [95%CI]	OR [95%CI]	OR [95%CI]	OR [95%CI]	OR [95%CI]	OR [95%CI]
Age (standardized)	1.92 [1.54, 2.36]	1.55 [1.23, 1.96]	1.06 [0.73, 1.54]	0.80 [0.63, 1.01]	0.93 [0.51, 1.60]	1.08 [0.80, 1.52]	1.13 [0.86, 1.54]
Male sex	1.28 [1.02, 1.59]	1.71 [1.10, 2.66]	1.10 [0.70, 1.76]	0.67 [0.34, 1.31]	0.82 [0.30, 2.10]	1.12 [0.76, 1.56]	1.02 [0.68, 1.44]
NA	1.15 [1.04, 1.28]	1.27 [1.07, 1.50]	1.13 [0.97, 1.34]	1.18 [0.94, 1.46]	1.29 [0.75, 1.98]	1.28 [1.13, 1.45]	1.26 [1.13, 1.43]
SI	1.01 [0.92, 1.13]	1.06 [0.87, 1.37]	1.08 [0.94, 1.26]	1.01 [0.83, 1.22]	0.98 [0.70, 1.35]	1.03 [0.92, 1.16]	1.03 [0.93, 1.16]
NA ²	1.04 [0.97, 1.11]	1.06 [0.93, 1.19]	1.07 [0.97, 1.18]	1.00 [0.82, 1.16]	1.04 [0.76, 1.37]	1.03 [0.95, 1.11]	1.02 [0.95, 1.10]
SI ²	1.01 [0.91, 1.09]	0.93 [0.81, 1.06]	1.08 [0.94, 1.28]	1.04 [0.86, 1.25]	1.09 [0.82, 1.45]	1.07 [0.97, 1.18]	1.05 [0.96, 1.13]
NA * SI (Type D)	0.99 [0.91, 1.09]	0.98 [0.84, 1.16]	1.08 [0.95, 1.25]	1.13 [0.82, 1.53]	1.15 [0.83, 1.65]	1.16 [1.01, 1.34]	1.20 [1.05, 1.36]

For bold faced cells the 95% Bayesian credible interval excludes an odds ratio of one

Bayes factors

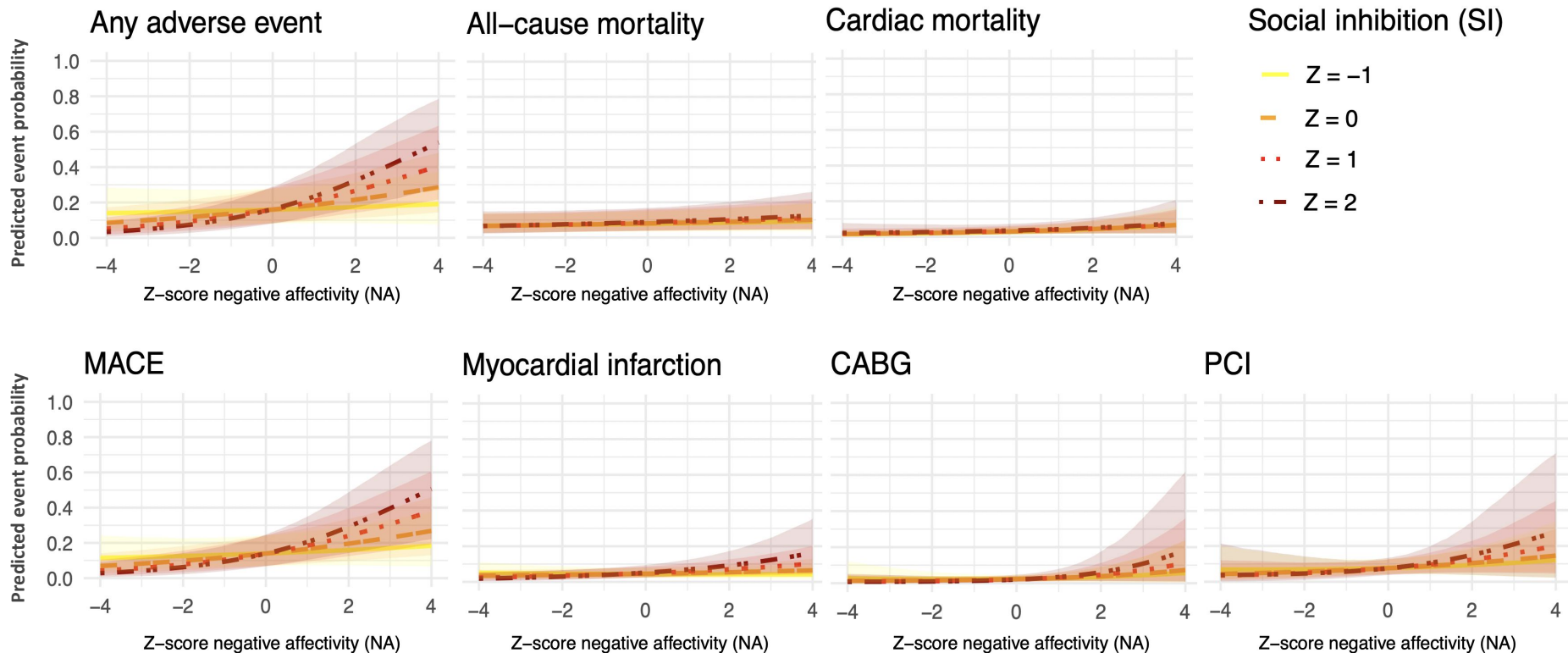
Type D effect	All-cause mortality		Cardiac mortality		Myocardial infarction		CABG		PCI		MACE		Any adverse event	
	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence	BF	Evidence
Complete sample (N=10759)														
Main hypothesis: $NA*SI > 0$	0.7	Anecdotal	0.7	Anecdotal	5.6	Substantial	4.2	Substantial	5.1	Substantial	42.5	Strong	129.4	Decisive
Null hypothesis: $NA*SI = 0$	45.9	Strong	23.7	Strong	16.9	Strong	8.8	Substantial	8.42	Substantial	3.1	Substantial	0.76	Anecdotal
CAD patients (N=7704)														
Main hypothesis: $NA*SI > 0$	3.8	Anecdotal	2.9	Anecdotal	4.5	Substantial	4.5	Substantial	5.8	Substantial	33.9	Strong	165.7	Decisive
Null hypothesis: $NA*SI = 0$	20.1	Strong	11.6	Strong	20.4	Strong	8.8	Substantial	8.6	Substantial	3.5	Substantial	0.8	Anecdotal
HF patients (N=2027) *														
Main hypothesis: $NA*SI > 0$	0.5	Anecdotal	0.8	Anecdotal	-		-		-		1.1	Anecdotal	1.2	Anecdotal
Null hypothesis: $NA*SI = 0$	10.1	Strong	5.4	Substantial	-		-		-		2.7	Anecdotal	2.6	Anecdotal

BF = Bayes factor; CABG = coronary artery bypass grafting; CAD = coronary artery disease; HF = heart failure; MACE = major adverse cardiac event; PCI = percutaneous coronary intervention

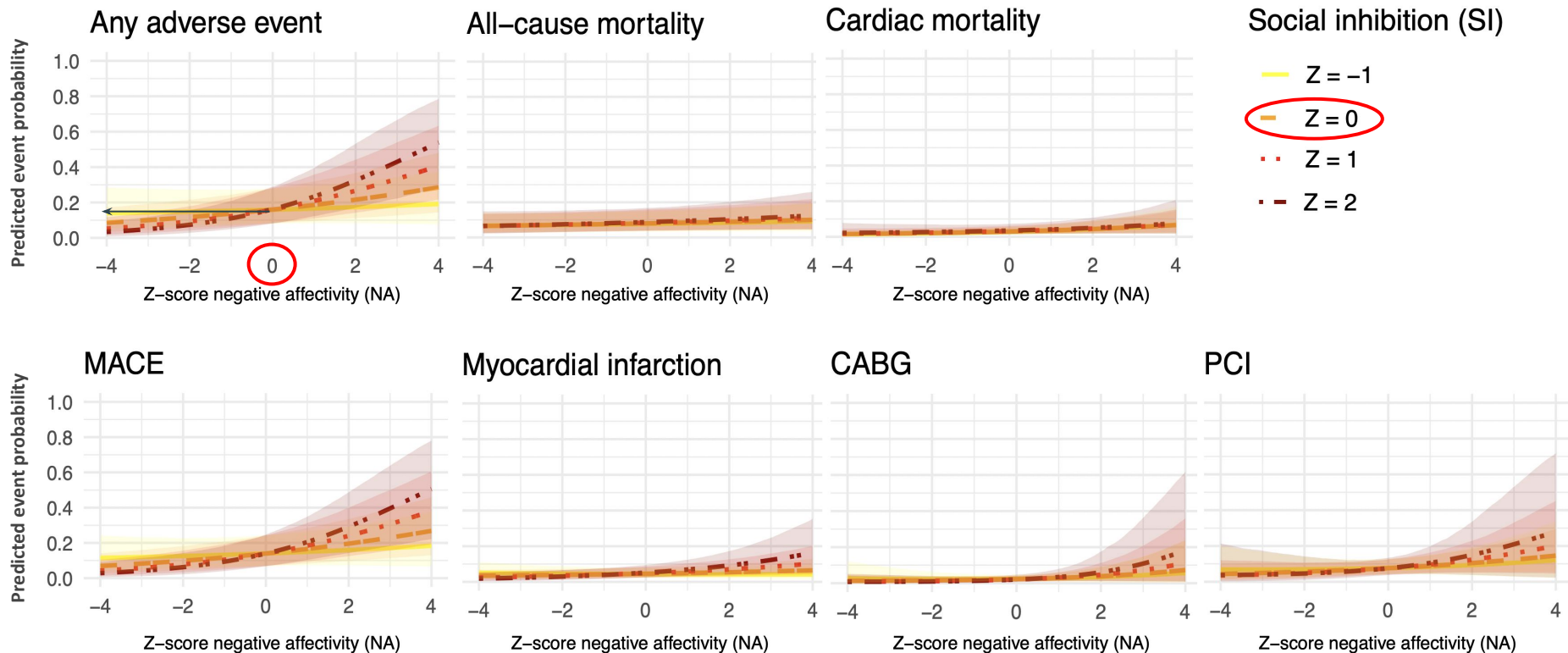
* Empty cells indicate that insufficient data was available to estimate the Type D effect on a particular endpoint for this patient sample

Bayes Factor	Interpretation
0-3	Anecdotal
3-10	Substantial
10-100	Strong
100+	Decisive

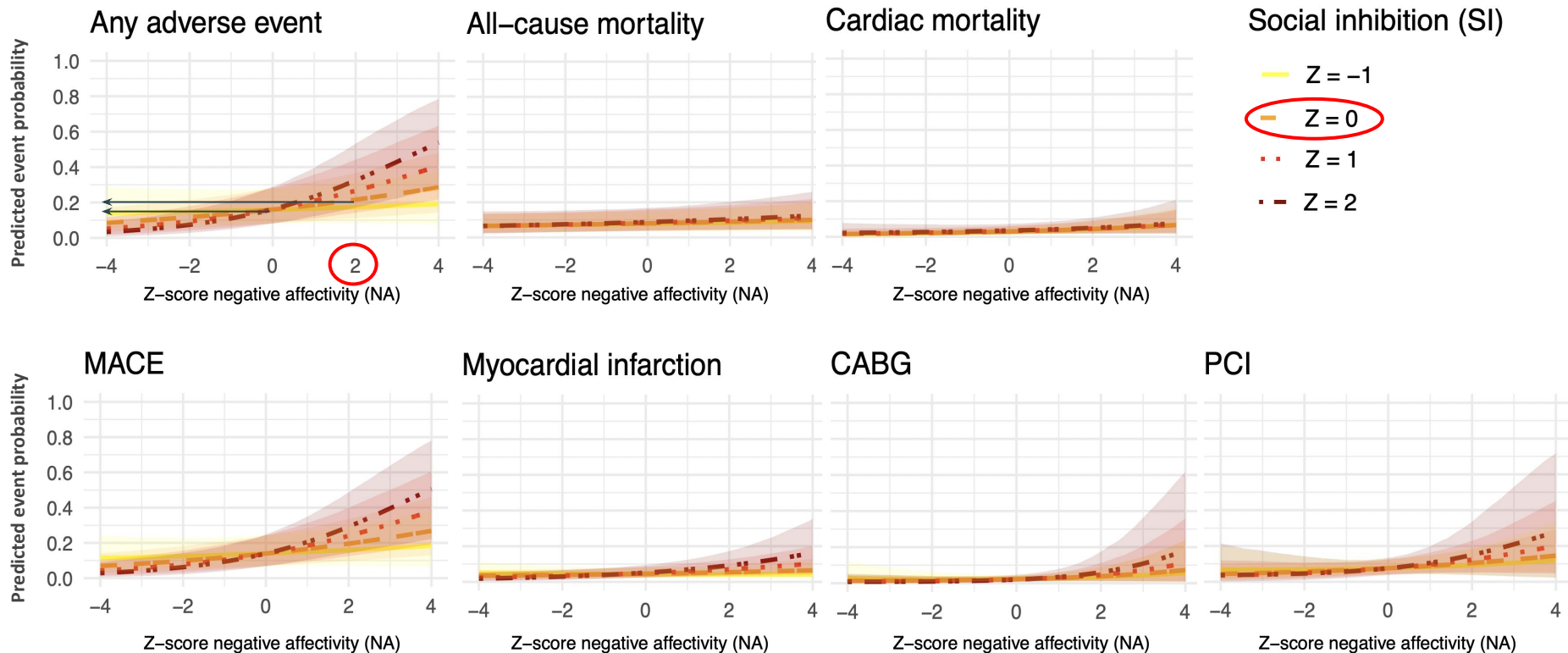
Type D personality effects



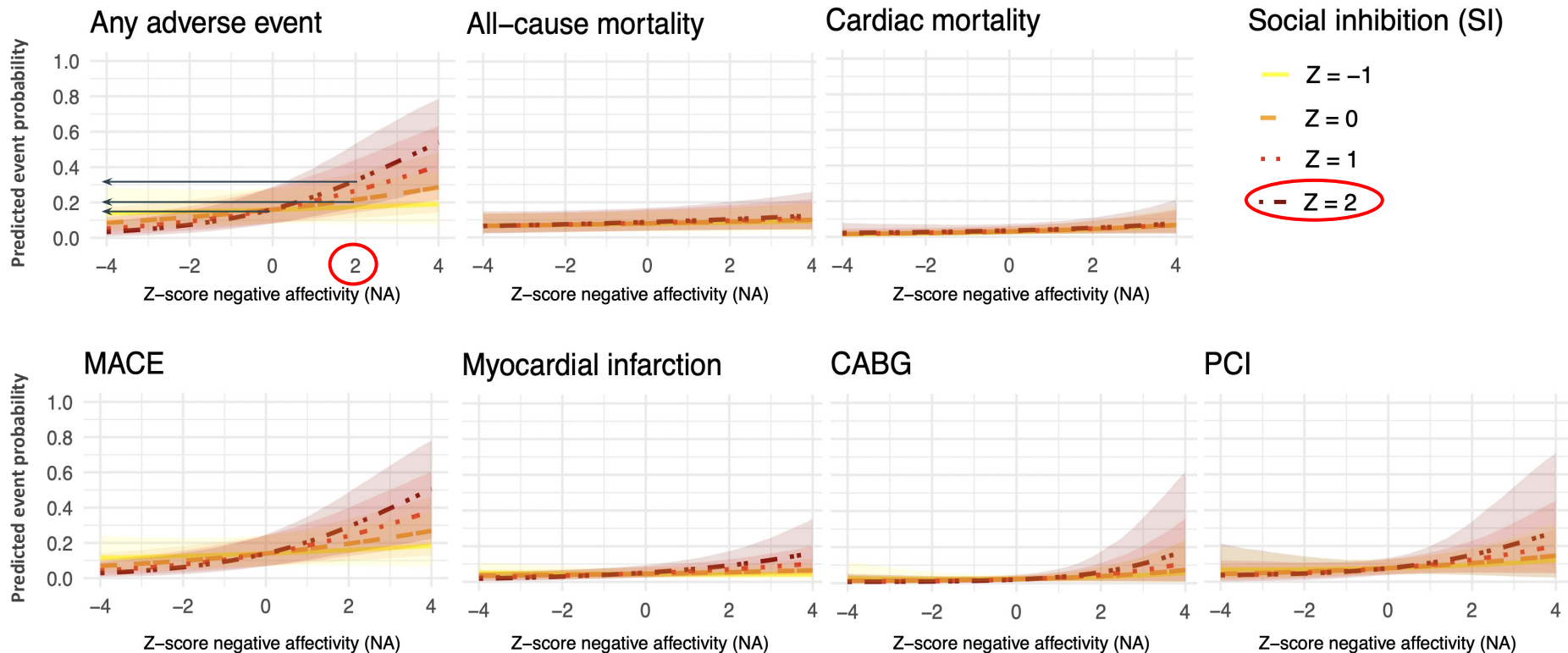
Type D personality effects



Type D personality effects



Type D personality effects



Do age and sex moderate the Type D effect?

Outcome	All-cause mortality	Cardiac mortality	Myocardial infarction	CABG	PCI	MACE	Any adverse event
Sample size	N = 10255	N = 5774	N = 5877	N = 2440	N = 2448	N = 3923	N = 3935
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							
Male sex * NA	1.052 [0.864, 1.283]	0.964 [0.591, 1.522]	0.96 [0.684, 1.348]	1.02 [0.593, 1.699]	1.299 [0.493, 3.25]	1.059 [0.756, 1.46]	1.006 [0.749, 1.352]
Male sex * SI2	0.946 [0.778, 1.154]	1.021 [0.649, 1.626]	1.019 [0.743, 1.424]	1.183 [0.707, 1.996]	0.766 [0.285, 1.908]	1.114 [0.808, 1.54]	1.04 [0.772, 1.392]
Male sex * NA2	1.181 [1.022, 1.361]	1.087 [0.81, 1.478]	1.117 [0.891, 1.413]	0.852 [0.579, 1.239]	0.611 [0.302, 1.131]	0.977 [0.791, 1.217]	1.003 [0.82, 1.243]
Male sex * SI2	1.005 [0.856, 1.169]	0.799 [0.591, 1.105]	1.071 [0.828, 1.384]	0.929 [0.608, 1.436]	0.677 [0.306, 1.427]	0.943 [0.753, 1.203]	0.99 [0.791, 1.256]
Male sex * NA * SI	0.984 [0.829, 1.162]	0.992 [0.676, 1.445]	0.998 [0.756, 1.314]	0.786 [0.451, 1.332]	1.753 [0.806, 3.65]	0.865 [0.625, 1.162]	0.858 [0.618, 1.153]
Moderating effect of age							
Age * NA	1.022 [0.899, 1.156]	0.972 [0.761, 1.256]	0.882 [0.747, 1.048]	0.984 [0.688, 1.565]	1.095 [0.693, 1.75]	0.987 [0.838, 1.154]	1.017 [0.858, 1.21]
Age * SI2	0.955 [0.853, 1.066]	0.989 [0.795, 1.235]	0.982 [0.831, 1.155]	1.131 [0.887, 1.47]	0.948 [0.61, 1.45]	0.949 [0.821, 1.092]	0.893 [0.775, 1.032]
Age * NA2	1.03 [0.95, 1.116]	1.12 [0.982, 1.287]	1.071 [0.936, 1.225]	1.041 [0.862, 1.266]	1.003 [0.71, 1.431]	1.063 [0.946, 1.194]	1.044 [0.934, 1.165]
Age * SI2	1.012 [0.933, 1.106]	1.115 [0.911, 1.346]	0.986 [0.864, 1.131]	0.922 [0.751, 1.154]	1.075 [0.726, 1.709]	1.02 [0.907, 1.163]	1.033 [0.91, 1.177]
Age * NA * SI	0.967 [0.879, 1.061]	0.948 [0.78, 1.18]	1.018 [0.873, 1.202]	0.848 [0.648, 1.1]	0.987 [0.661, 1.48]	0.965 [0.82, 1.133]	0.959 [0.813, 1.144]

CABG = coronary artery bypass grafting; MACE = major adverse cardiac event; OR = Odds ratio; PCI = percutaneous coronary intervention

4

Limitations & future research

- Limitations
 - 7 of 25 (28%) eligible studies did not participate
 - No unpublished studies included
 - No clinical covariates
- Future research
 - More individual patient data meta-analyses
 - Study underlying biological mechanism

5

Conclusion

- Type D predicts MACE & any adverse event in coronary artery disease patients
- NA (and not Type D) predicts all-cause & cardiac mortality
- No Type D effect in heart failure patients

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Co-authors (participating studies)

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Dr. D.J. van Veldhuisen
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Dr. Jelte Wicherts



Dr. Johan Denollet[†]



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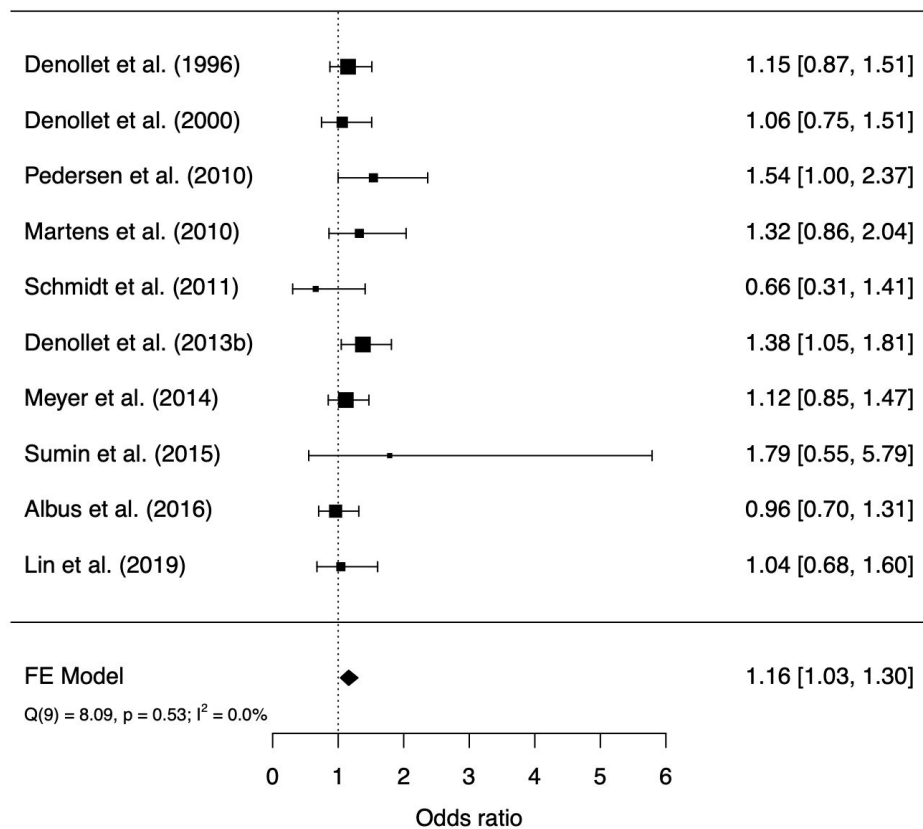
Any questions?

You can contact me at:

- p.lodder@uvt.nl
- www.paultwin.com

Two-step individual patient data meta-analysis

Major adverse cardiac events



Main effects and Interaction effects of NA and SI subtraits

			SOCIAL INHIBITION						
			Inhibited in social interactions (DS6)	Difficulties starting a conversation (DS8)	Does not find things to talk about (DS14)	Closed kind of person (DS10)	Keeps others at a distance (DS11)	Makes contact easily (DS1)	Often talks to strangers (DS3)
			Discomfort in social situations			Reticence		Lack of social poise	
NEGATIVE AFFECTIVITY	Often feels unhappy (DS4)	Dysphoria	NA = 0.32 ***			NA = 0.27 ***		NA = 0.28 ***	
	Takes gloomy view of things (DS7)								
	Is often down in the dumps (DS13)								
	Worries about unimportant things (DS2)	Anxious apprehension	-			NA x SI = 0.14 *		NA x SI = 0.15 *	
Often worries about something (DS12)									
	Is easily irritated (DS5)	Irritability	NA = 0.21 **			NA = 0.19 *		NA = 0.20 **	
	Is often in a bad mood (DS9)								

Interaction effects between individual NA & SI items

		SOCIAL INHIBITION						
		Makes contact easily (DS1)	Often talks to strangers (DS3)	Inhibited in social interactions (DS6)	Difficulties starting a conversation (DS8)	Closed kind of person (DS10)	Keeps others at a distance (DS11)	Does not find things to talk about (DS14)
NEGATIVE AFFECTIVITY	Worries about unimportant things (DS2)	0.09*	0.081*	0.016	0.019	0.055	0.088*	0.074
	Often feels unhappy (DS4)	0.085	0.043	0.003	0.031	0.068	0.068	0.046
	Is easily irritated (DS5)	0.023	0.03	0.015	0.019	0.009	0.089*	0.042
	Takes gloomy view of things (DS7)	0.089	-0.014	0.021	0.035	0.021	0.096*	0.02
	Is often in a bad mood (DS9)	0.025	-0.049	0.023	0.014	-0.025	0.012	0.006
	Often worries about something (DS12)	0.072	0.041	0.014	0.028	0.046	0.073	0.052
	Is often down in the dumps (DS13)	0.047	-0.004	0.013	-0.006	0.008	0.097*	0.001