# SUPPLEMENTARY MATERIAL to:

# Advancing the Personalized Advantage Index (PAI): a Systematic Review and Application in Two Large Multi-Site Samples in Anxiety Disorders.

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# Supplement A

Table A1

Tailored questions to examine risk of bias

|  |  |  |  |
| --- | --- | --- | --- |
| Question | Low ROB | Medium ROB | High ROB |
| 4.8.1 “What is the extent of risk of bias introduced by the cross-validation procedure?” | * external/holdout CV AND test set size > 100
* repeated k-folds CV AND sample size > 100
 | * external/holdout CV AND test set size ≤ 100
* repeated k-folds CV AND sample size ≤ 100
* non-repeated k-folds CV
 | * LOO CV
 |
| 4.8.2 “What is the extent of risk of bias introduced by (not) integrating preprocessing steps into the CV?” | All steps of model development occurred in the CV | Feature imputation and feature scaling occurred outside the CV | Feature selection occurred outside the CV |

*Note.* Abbreviations:ROB = risk of bias, CV = cross-validation, LOO = leave-one-out

# Supplement B

Table B1

PROBAST Rating

| Question | Ahuvia, 2023 | Bremer, 2023 | Brujniks, 2022 | Cohen, 2020 | Deisenhofer, 2018 | DeRubeis, 2014 | Friedl, Berger, 2020 | Friedl, Krieger, 2020 | Hautmann, 2023; ADHD symptoms | Hautmann, 2023; ODD symptoms | Held, 2023 | Hoeboer, 2021; CAPS-5, PCL-5 | Huibers, 2015 | Keefe, 2021; initial model | Keefe, 2021; less biased model | Loohuis, 2022 | Lopez-Gomez, 2019 | Schwartz, 2021 | Senger, 2021 | van Bronswijk, 2021; FreqMesh, STEPd | van Bronswijk, 2021; cross-trial | Webb, 2019 |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1.1 Were appropriate data sources used, e.g., cohort, RCT, or nested case–control study data? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 1.2 Were all inclusions and exclusions of participants appropriate? | Y | N | Y | Y | Y | N | Y | N | Y | Y | Y | Y | N | N | N | NI | N | Y | Y | Y | Y | N |
| Final rating domain 1 (risk of bias) | low | high | low | low | low | high | low | high | low | low | low | low | high | high | high | low | high | low | low | low | high | high |
| 2.1 Were predictors defined and assessed in a similar way for all participants? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 2.2 Were predictor assessments made without knowledge of outcome data? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 2.3 Are all predictors available at the time the model is intended to be used? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| Final rating domain 2 (risk of bias) | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low |
| 3.1 Was the outcome determined appropriately? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 3.2 Was a prespecified or standard outcome definition used?  | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 3.3 Were predictors excluded from the outcome definition?  | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 3.4 Was the outcome defined and determined in a similar way for all participants? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 3.5 Was the outcome determined without knowledge of predictor information?  | N | NI | N | N | N | Y | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | Y |
| 3.6 Was the time interval between predictor assessment and outcome determination appropriate? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| Final rating domain 3 (risk of bias) | low | low | low | low | high | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low | low |
| 4.1 Were there a reasonable number of participants with the outcome?  | N | N | N | N | N | N | N | N | N | N | Y | N | N | N | N | Y | N | Y | N | N | Y | N |
| 4.2 Were continuous and categorical predictors handled appropriately?  | Y | Y | Y | Y | Y | Y | Y | NI | Y | Y | NI | NI | Y | NI | NI | Y | Y | Y | Y | Y | Y | Y |
| 4.3 Were all enrolled participants included in the analysis? | N | N | Y | N | N | N | N | N | N | N | N | Y | N | N | N | Y | N | N | N | Y | Y | N |
| 4.4 Were participants with missing data handled appropriately? | Y | N | N | N | Y | NI | Y | Y | N | N | N | NI | N | Y | Y | N | Y | Y | N | N | N | N |
| 4.5 Was selection of predictors based on univariable analysis avoided? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | Y | NA | Y |
| 4.6 Were complexities in the data (e.g., censoring, competing risks, sampling of control participants) accounted for appropriately? | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| 4.7 Were relevant model performance measures evaluated appropriately? | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | Y | N | N | N | N | N | N |
| 4.8.1 What is the extent of ROB introduced by the cross-validation procedure? | low | medium | medium | low | high | high | high | high | high | high | high | high | high | low | medium | medium | medium | low | high | medium | low | low |
| 4.8.2 What is the extent of ROB introduced by (not) integrating preprocessing steps into the CV? | low | high | high | high | high | high | high | high | high | high | high | high | high | high | medium | high | high | low | high | medium | low | high |
| 4.8 Were model overfitting and optimism in model performance accounted for? | Y | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | Y | N | N | NA | N |
| 4.9 Do predictors and their assigned weights in the final model correspond to the results from the reported multivariable analysis? (development studies only) | NI | NI | NI | NI | NI | NI | NI | NI | Y | Y | NI | NI | NI | NI | N | NI | NI | NI | NI | NI | NA | NI |
| Final rating domain 4 (risk of bias) | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high |
| Final rating (risk of bias) | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high | high |

Note. We performed a PROBAST rating for each subanalysis but combined subanalyses here if the rating did not differ to enhance readability. Abbreviations: ROB = risk of bias, CV = cross validation.

Figure B1

PROBAST rating overview



# Supplement C

Table C1

Sample statistics for all variables initially considered as predictors and treatment outcome in PANIC-Net

| **Variable** | **NA** | **Therapist-guided exposures**, N = 142*1* | **Unguided exposures**, N = 119*1* | **All**, N = 261*1* |
| --- | --- | --- | --- | --- |
| **Female** | 0 | 105 (74 %) | 92 (77 %) | 197 (75 %) |
| **Age** | 0 | 35 (11) | 36 (11) | 36 (11) |
| **Employment** | 0 |  |  |  |
|     University |  | 7 (4.9 %) | 4 (3.4 %) | 11 (4.2 %) |
|     Job training |  | 33 (23 %) | 31 (26 %) | 64 (25 %) |
|     Employed |  | 85 (60 %) | 70 (59 %) | 155 (59 %) |
|     Unemployed |  | 16 (11 %) | 13 (11 %) | 29 (11 %) |
|     Other |  | 1 (0.7 %) | 1 (0.8 %) | 2 (0.8 %) |
| **Years of education** | 0 |  |  |  |
|     8 |  | 17 (12 %) | 11 (9.2 %) | 28 (11 %) |
|     10 |  | 56 (39 %) | 56 (47 %) | 112 (43 %) |
|     12-13 |  | 64 (45 %) | 51 (43 %) | 115 (44 %) |
|     No formal degree |  | 5 (3.5 %) | 1 (0.8 %) | 6 (2.3 %) |
| **Living arrangement** | 0 |  |  |  |
|     With parents |  | 10 (7.0 %) | 5 (4.2 %) | 15 (5.7 %) |
|     Alone |  | 29 (20 %) | 19 (16 %) | 48 (18 %) |
|     With partner |  | 98 (69 %) | 84 (71 %) | 182 (70 %) |
|     Other |  | 5 (3.5 %) | 11 (9.2 %) | 16 (6.1 %) |
| **Marital status** | 1 |  |  |  |
|     Married |  | 49 (35 %) | 38 (32 %) | 87 (33 %) |
|     Divorced/widowed/separated |  | 15 (11 %) | 17 (14 %) | 32 (12 %) |
|     Never married |  | 78 (55 %) | 63 (53 %) | 141 (54 %) |
| **Social class** | 5 |  |  |  |
|     Lowest |  | 5 (3.6 %) | 8 (6.8 %) | 13 (5.1 %) |
|     Lower middle |  | 37 (27 %) | 20 (17 %) | 57 (22 %) |
|     Middle |  | 83 (60 %) | 72 (62 %) | 155 (61 %) |
|     Upper middle |  | 14 (10 %) | 17 (15 %) | 31 (12 %) |
| **Any harmful alcohol use** | 0 | 51 (36 %) | 51 (43 %) | 102 (39 %) |
| **Alcohol abuse** | 0 | 9 (6.3 %) | 7 (5.9 %) | 16 (6.1 %) |
| **Alcohol dependence** | 0 | 2 (1.4 %) | 0 (0 %) | 2 (0.8 %) |
| **Nicotine dependence** | 0 | 43 (30 %) | 32 (27 %) | 75 (29 %) |
| **Any illicit substance abuse** | 0 | 0 (0 %) | 0 (0 %) | 0 (0 %) |
| **Any illicit substance dependence** | 0 | 0 (0 %) | 0 (0 %) | 0 (0 %) |
| **# psychotic symptoms** | 0 | 1.87 (2.21) | 1.42 (1.84) | 1.66 (2.06) |
| **Possible psychotic disorder** | 0 | 20 (14 %) | 10 (8.4 %) | 30 (11 %) |
| **Any sin/rec depressive disorder** | 0 | 56 (39 %) | 35 (29 %) | 91 (35 %) |
| **Any dysthymia/depressive disorder** | 0 | 66 (46 %) | 42 (35 %) | 108 (41 %) |
| **Any somatoform/conv. syndrom** | 0 | 41 (29 %) | 34 (29 %) | 75 (29 %) |
| **Any somatoform/conv. disorder** | 0 | 57 (40 %) | 35 (29 %) | 92 (35 %) |
| **Any eating disorder** | 0 | 0 (0 %) | 0 (0 %) | 0 (0 %) |
| **Disorder due to GMC** | 0 | 4 (2.8 %) | 5 (4.2 %) | 9 (3.4 %) |
| **Social phobia** | 0 | 59 (42 %) | 45 (38 %) | 104 (40 %) |
| **Any simple phobia** | 0 | 103 (73 %) | 79 (66 %) | 182 (70 %) |
| **Generalized anxiety disorder** | 0 | 26 (18 %) | 27 (23 %) | 53 (20 %) |
| **Obsessive-compulsive disorder** | 0 | 14 (9.9 %) | 13 (11 %) | 27 (10 %) |
| **Any qualified trauma** | 0 | 39 (27 %) | 33 (28 %) | 72 (28 %) |
| **Any trauma** | 0 | 45 (32 %) | 45 (38 %) | 90 (34 %) |
| **Posttraumatic stress disorder** | 0 | 5 (3.5 %) | 1 (0.8 %) | 6 (2.3 %) |
| **AAQ-II** | 1 | 44 (10) | 47 (10) | 45 (10) |
| **ACQ total** | 0 | 2.17 (0.53) | 2.17 (0.55) | 2.17 (0.54) |
| **ACQ (loss of control)** | 0 | 2.11 (0.73) | 2.06 (0.69) | 2.09 (0.71) |
| **ACQ (physical concerns)** | 0 | 2.24 (0.67) | 2.28 (0.69) | 2.26 (0.68) |
| **ASI** | 0 | 32 (12) | 30 (11) | 31 (11) |
| **BAT - group** | 3 |  |  |  |
|     low anxious non-escapers |  | 82 (59 %) | 56 (47 %) | 138 (53 %) |
|     high anxious non-escapers |  | 21 (15 %) | 21 (18 %) | 42 (16 %) |
|     escapers |  | 26 (19 %) | 23 (19 %) | 49 (19 %) |
|     avoiders |  | 11 (7.9 %) | 18 (15 %) | 29 (11 %) |
| **BDI-II** | 0 | 17 (9) | 15 (8) | 16 (9) |
| **BSI GSI** | 0 | 1.17 (0.56) | 1.05 (0.53) | 1.11 (0.55) |
| **BSI total** | 0 | 1.97 (0.49) | 1.90 (0.46) | 1.94 (0.48) |
| **BSI (somatization)** | 0 | 1.27 (0.72) | 1.21 (0.80) | 1.25 (0.76) |
| **BSI (obsessive compulsive)** | 0 | 1.01 (0.64) | 0.96 (0.65) | 0.99 (0.65) |
| **BSI (interpersonal sensitivity)** | 0 | 1.15 (0.84) | 0.98 (0.83) | 1.07 (0.84) |
| **BSI (depression)** | 0 | 1.03 (0.73) | 0.86 (0.69) | 0.95 (0.72) |
| **BSI (anxiety)** | 0 | 1.72 (0.83) | 1.60 (0.83) | 1.67 (0.83) |
| **BSI (hostility)** | 0 | 0.77 (0.68) | 0.64 (0.59) | 0.71 (0.64) |
| **BSI (phobic anxiety)** | 0 | 2.02 (0.98) | 1.89 (1.06) | 1.96 (1.02) |
| **BSI (paranoid ideation)** | 0 | 0.77 (0.74) | 0.63 (0.68) | 0.70 (0.72) |
| **BSI (psychoticism)** | 0 | 0.69 (0.58) | 0.59 (0.54) | 0.64 (0.56) |
| **BSI (additional items)** | 0 | 1.04 (0.79) | 0.87 (0.68) | 0.96 (0.75) |
| **BSQ** | 0 | 48 (12) | 48 (13) | 48 (12) |
| **CGI - pre baseline** | 0 | 5.00 (4.00-7.00) | 5.00 (4.00-7.00) | 5.00 (4.00-7.00) |
| **CGI - baseline** | 0 | 5.00 (2.00-7.00) | 5.00 (4.00-7.00) | 5.00 (2.00-7.00) |
| **CLQ total** | 0 | 56 (21) | 57 (21) | 56 (21) |
| **CLQ (suffocation)** | 0 | 26 (11) | 27 (11) | 27 (11) |
| **CLQ (restriction)** | 0 | 30 (12) | 29 (12) | 30 (12) |
| **EQ5** | 1 | 0.62 (0.14) | 0.62 (0.16) | 0.62 (0.15) |
| **IPAQ total** | 21 | 6,267 (9,035) | 5,649 (6,773) | 5,984 (8,067) |
| **IPAQ (work)** | 117 | 2,237 (3,909) | 2,108 (4,707) | 2,175 (4,295) |
| **IPAQ (transportation)** | 21 | 1,273 (3,625) | 1,001 (1,449) | 1,149 (2,841) |
| **IPAQ (domestic)** | 21 | 2,108 (2,721) | 2,143 (2,837) | 2,124 (2,769) |
| **IPAQ (leisure)** | 21 | 1,595 (3,248) | 1,184 (1,481) | 1,406 (2,595) |
| **HAMA total** | 0 | 23 (7) | 23 (7) | 23 (7) |
| **HAMA (psychic)** | 0 | 13.0 (4.3) | 13.1 (4.0) | 13.1 (4.2) |
| **HAMA (somatic)** | 0 | 10.2 (4.7) | 10.2 (4.6) | 10.2 (4.6) |
| **MI (accompanied)** | 25 | 2.27 (0.76) | 2.22 (0.69) | 2.25 (0.73) |
| **MI (alone)** | 25 | 3.00 (0.84) | 2.89 (0.79) | 2.95 (0.82) |
| **PAS total** | 0 | 28 (10) | 27 (10) | 28 (10) |
| **PAS (agoraphobis avoidance)** | 0 | 2.05 (1.03) | 2.03 (1.03) | 2.04 (1.03) |
| **PAS (anticipatory anxiety)** | 0 | 2.62 (0.95) | 2.61 (0.97) | 2.61 (0.96) |
| **PAS (disability)** | 0 | 1.65 (0.95) | 1.59 (0.94) | 1.62 (0.94) |
| **PAS (health worries)** | 0 | 1.68 (1.21) | 1.72 (1.08) | 1.70 (1.15) |
| **PANAS (positive)** | 2 | 16 (7) | 17 (7) | 16 (7) |
| **PANAS (negative)** | 2 | 16 (7) | 15 (7) | 16 (7) |
| **SDS** | 2 | 12 (6) | 12 (7) | 12 (7) |
| **SPA** | 1 | 2.29 (0.66) | 2.27 (0.70) | 2.28 (0.68) |
| **HAMA total post-treatment** | 0 | 13 (8) | 13 (7) | 13 (8) |
| *1*n (% %); Mean (SD); Median (Minimum-Maximum) |

Note. Variables are presented in the following order: sociodemographic variables, disorder-related variables, questionnaire and behavioral variables. All diagnoses are 12-month diagnoses. Abbreviations: NA = missings, # = number, AAQ-II = acceptance and action questionnaire-II, ACQ = agoraphobic cognitions questionnaire, ASI = anxiety sensitivity index, BAT = Behavioral Avoidance Test, BDI-II = Beck depression inventory-II, BSI = brief symptom inventory, BSI-GSI = BSI sum score divided by #items >0, BSQ = bodily sensations questionnaire, CGI = clinical global index, CLQ = claustrophobia questionnaire, EQ5 = Health Related Quality of Life, HAMA = Hamilton Anxiety Scale, IPAQ = international physiological activity questionnaire, MI = mobility inventory, PANAS = positive and negative affect schedule, PAS = panic and agoraphobia scale, SDS = Sheen disability scale, SPA = self-made questionnaire measuring symptoms during a panic attack.

Table C2

Sample statistics for all variables initially considered as predictors and treatment outcome in Protect-AD

| **Variable** | **NA** | **Standard non-intensified exposure**, N = 307*1* | **Temporally intensified exposure**, N = 307*1* | **ALL**, N = 614*1* |
| --- | --- | --- | --- | --- |
| **Female** | 0 | 160 (52 %) | 181 (59 %) | 341 (56 %) |
| **Age** | 0 | 34 (12) | 32 (11) | 33 (12) |
| **Employment** | 82 |  |  |  |
|     Employed |  | 219 (85 %) | 205 (75 %) | 424 (80 %) |
|     Student |  | 29 (11 %) | 44 (16 %) | 73 (14 %) |
|     Job training |  | 5 (1.9 %) | 8 (2.9 %) | 13 (2.4 %) |
|     Unemployed |  | 6 (2.3 %) | 16 (5.9 %) | 22 (4.1 %) |
|     Other |  | 0 (0 %) | 0 (0 %) | 0 (0 %) |
| **Living arragement** | 0 |  |  |  |
|     Alone |  | 133 (43 %) | 126 (41 %) | 259 (42 %) |
|     With partner |  | 72 (23 %) | 60 (20 %) | 132 (21 %) |
|     With parents |  | 41 (13 %) | 57 (19 %) | 98 (16 %) |
|     Other |  | 61 (20 %) | 64 (21 %) | 125 (20 %) |
| **Marital status** | 0 |  |  |  |
|     Married |  | 69 (22 %) | 61 (20 %) | 130 (21 %) |
|     Divorced/widowed/seperated |  | 30 (9.8 %) | 19 (6.2 %) | 49 (8.0 %) |
|     Never married |  | 208 (68 %) | 227 (74 %) | 435 (71 %) |
| **Social class** | 0 |  |  |  |
|     Lower class |  | 13 (4.2 %) | 19 (6.2 %) | 32 (5.2 %) |
|     Lower-middle class |  | 79 (26 %) | 66 (21 %) | 145 (24 %) |
|     Middle class |  | 180 (59 %) | 175 (57 %) | 355 (58 %) |
|     Upper-middle class |  | 33 (11 %) | 45 (15 %) | 78 (13 %) |
|     Upper class |  | 1 (0.3 %) | 1 (0.3 %) | 2 (0.3 %) |
|     No class |  | 1 (0.3 %) | 1 (0.3 %) | 2 (0.3 %) |
| **Living situation** | 10 |  |  |  |
|     Metropolitan |  | 167 (56 %) | 186 (61 %) | 353 (58 %) |
|     Smalltown |  | 70 (23 %) | 58 (19 %) | 128 (21 %) |
|     Rural |  | 63 (21 %) | 60 (20 %) | 123 (20 %) |
| **BMI** | 5 | 25.0 (5.1) | 24.1 (5.1) | 24.5 (5.1) |
| **Weight** | 5 |  |  |  |
|     Underweight |  | 11 (3.6 %) | 20 (6.6 %) | 31 (5.1 %) |
|     Normalweight |  | 171 (56 %) | 185 (61 %) | 356 (58 %) |
|     Overweight |  | 122 (40 %) | 100 (33 %) | 222 (36 %) |
| **Primary disorder** | 0 |  |  |  |
|     Agoraphobia |  | 22 (7.2 %) | 16 (5.2 %) | 38 (6.2 %) |
|     Agoraphobia with panic disorder |  | 135 (44 %) | 132 (43 %) | 267 (43 %) |
|     Panic disorder |  | 28 (9.1 %) | 36 (12 %) | 64 (10 %) |
|     Social anxiety |  | 95 (31 %) | 92 (30 %) | 187 (30 %) |
|     Specific phobias |  | 27 (8.8 %) | 31 (10 %) | 58 (9.4 %) |
| **Primary disorder age of onset** | 115 | 20 (12) | 19 (11) | 20 (11) |
| **Primary disorder duration** | 115 | 14 (12) | 14 (11) | 14 (12) |
| **Alcohol abuse** | 0 | 3 (1.0 %) | 2 (0.7 %) | 5 (0.8 %) |
| **Alcohol dependence** | 0 | 12 (3.9 %) | 11 (3.6 %) | 23 (3.7 %) |
| **Nicotine dependence** | 0 | 72 (23 %) | 67 (22 %) | 139 (23 %) |
| **Possible psychotic disorder** | 0 | 6 (2.0 %) | 3 (1.0 %) | 9 (1.5 %) |
| **Any sin/rec depressive disorder** | 0 | 112 (36 %) | 118 (38 %) | 230 (37 %) |
| **Any dysthymia/depressive disorder** | 0 | 58 (19 %) | 69 (22 %) | 127 (21 %) |
| **Agoraphobia without panic attack** | 0 | 42 (14 %) | 25 (8.1 %) | 67 (11 %) |
| **Panic disorder with agoraphobia** | 0 | 166 (54 %) | 175 (57 %) | 341 (56 %) |
| **Social phobia** | 0 | 167 (54 %) | 157 (51 %) | 324 (53 %) |
| **Generalized anxiety disorder** | 0 | 49 (16 %) | 49 (16 %) | 98 (16 %) |
| **Panic disorder** | 0 | 0.11 (0.31) | 0.12 (0.33) | 0.12 (0.32) |
| **Specific phobia: animal type** | 0 | 33 (11 %) | 46 (15 %) | 79 (13 %) |
| **Specific phobia: natural environment type** | 0 | 56 (18 %) | 69 (22 %) | 125 (20 %) |
| **Specific phobia: blood injection injury type** | 0 | 46 (15 %) | 49 (16 %) | 95 (15 %) |
| **Specific phobia: situational type** | 0 | 90 (29 %) | 77 (25 %) | 167 (27 %) |
| **Specific phobia: other type** | 0 | 39 (13 %) | 44 (14 %) | 83 (14 %) |
| **Obsessive-compulsive disorder** | 0 | 41 (13 %) | 33 (11 %) | 74 (12 %) |
| **Posttraumatic stress disorder** | 0 | 8 (2.6 %) | 5 (1.6 %) | 13 (2.1 %) |
| **# diagnoses** | 0 | 3.89 (1.90) | 3.96 (1.90) | 3.93 (1.90) |
| **First disorder age of onset** | 51 | 16 (11) | 15 (11) | 15 (11) |
| **Previous treatments** | 0 |  |  |  |
|     None |  | 156 (51 %) | 150 (49 %) | 306 (50 %) |
|     Psychotherapy |  | 65 (21 %) | 76 (25 %) | 141 (23 %) |
|     Medication |  | 0 (0 %) | 0 (0 %) | 0 (0 %) |
|     Inpatient treatment |  | 86 (28 %) | 81 (26 %) | 167 (27 %) |
| **# previous treatments** | 0 |  |  |  |
|     0 |  | 127 (41 %) | 131 (43 %) | 258 (42 %) |
|     > 1 |  | 75 (24 %) | 90 (29 %) | 165 (27 %) |
|     2 + |  | 105 (34 %) | 86 (28 %) | 191 (31 %) |
| **AAQ** | 0 | 43 (11) | 43 (11) | 43 (11) |
| **ACQ total** | 0 | 1.95 (0.54) | 1.97 (0.52) | 1.96 (0.53) |
| **ACQ (loss of control)** | 0 | 2.11 (0.72) | 2.10 (0.72) | 2.10 (0.72) |
| **ACQ (physical concerns)** | 0 | 1.80 (0.68) | 1.85 (0.67) | 1.82 (0.67) |
| **ASI** | 0 | 27 (11) | 27 (11) | 27 (11) |
| **BIS** | 0 | 33 (6) | 32 (6) | 32 (6) |
| **BIS (non-planning)** | 0 | 11.4 (3.3) | 11.2 (3.1) | 11.3 (3.2) |
| **BIS (motor)** | 0 | 10.18 (3.00) | 10.25 (2.88) | 10.21 (2.94) |
| **BIS (attentional)** | 0 | 11.04 (2.78) | 10.86 (2.66) | 10.95 (2.72) |
| **BIS-BAS (inhibition)** | 0 | 3.38 (0.47) | 3.37 (0.48) | 3.37 (0.47) |
| **BIS-BAS (approach)** | 0 | 2.75 (0.42) | 2.75 (0.41) | 2.75 (0.42) |
| **BIS-BAS (drive)** | 0 | 2.69 (0.60) | 2.70 (0.54) | 2.69 (0.57) |
| **BIS-BAS (fun seeking)** | 0 | 2.63 (0.54) | 2.61 (0.55) | 2.62 (0.54) |
| **BIS-BAS (reward)** | 0 | 2.90 (0.47) | 2.90 (0.47) | 2.90 (0.47) |
| **BSI GSI** | 0 | 1.65 (0.44) | 1.70 (0.43) | 1.67 (0.44) |
| **BSI total** | 0 | 0.94 (0.55) | 0.98 (0.52) | 0.96 (0.54) |
| **BSI (somatization)** | 0 | 0.82 (0.66) | 0.84 (0.62) | 0.83 (0.64) |
| **BSI (obsessive compulsive)** | 0 | 0.98 (0.68) | 1.03 (0.67) | 1.01 (0.67) |
| **BSI (interpersonal sensitivity)** | 0 | 1.21 (0.95) | 1.31 (1.00) | 1.26 (0.98) |
| **BSI (depression)** | 0 | 0.97 (0.81) | 1.08 (0.82) | 1.03 (0.82) |
| **BSI (anxiety)** | 0 | 1.24 (0.73) | 1.24 (0.65) | 1.24 (0.69) |
| **BSI (hostility)** | 0 | 0.66 (0.60) | 0.69 (0.58) | 0.67 (0.59) |
| **BSI (phobic anxiety)** | 0 | 1.12 (0.88) | 1.07 (0.79) | 1.09 (0.83) |
| **BSI (paranoid ideation)** | 0 | 0.75 (0.73) | 0.82 (0.75) | 0.79 (0.74) |
| **BSI (psychoticism)** | 0 | 0.70 (0.66) | 0.76 (0.66) | 0.73 (0.66) |
| **BSI (additional items)** | 0 | 0.82 (0.65) | 0.92 (0.70) | 0.87 (0.67) |
| **BDI** | 0 | 16 (10) | 17 (10) | 17 (10) |
| **BSQ** | 0 | 2.40 (0.70) | 2.43 (0.63) | 2.41 (0.67) |
| **CGI (total)** | 0 | 5 (4-6) | 5 (4-7) | 5 (4-7) |
| **CGI (depression)** | 0 | 5 (2-6) | 5 (2-6) | 5 (2-6) |
| **CGI (anxiety)** | 0 | 4 (2-6) | 5 (2-6) | 4 (2-6) |
| **CGI (avoidance)** | 0 | 5 (1-6) | 5 (2-7) | 5 (1-7) |
| **CGI (functioning)** | 0 | 4 (1-6) | 4 (2-6) | 4 (1-6) |
| **CTS** | 0 | 2.48 (3.01) | 2.54 (3.20) | 2.51 (3.10) |
| **DSM-5 Cross-D** | 0 | 15 (8) | 16 (7) | 16 (7) |
| **DSM-5 SP** | 0 | 16 (11) | 15 (10) | 16 (10) |
| **EQ5** | 0 | 0.66 (0.15) | 0.65 (0.14) | 0.66 (0.14) |
| **ERQ (reappraisal)** | 0 | 4.00 (1.13) | 3.98 (1.05) | 3.99 (1.09) |
| **ERQ (suppression)** | 0 | 4.05 (1.27) | 3.93 (1.21) | 3.99 (1.24) |
| **GAD7** | 1 | 9.3 (4.7) | 9.3 (4.4) | 9.3 (4.5) |
| **HAMA total** | 0 | 24.3 (5.4) | 24.6 (5.3) | 24.4 (5.3) |
| **HAMA (psychic)** | 0 | 14.7 (3.4) | 14.9 (3.5) | 14.8 (3.4) |
| **HAMA (somatic)** | 0 | 9.6 (4.0) | 9.7 (3.9) | 9.6 (4.0) |
| **LSAS** | 0 | 48 (30) | 47 (31) | 48 (31) |
| **LSAS (performance anxiety)** | 0 | 26 (16) | 25 (16) | 25 (16) |
| **LSAS (performance social situations)** | 0 | 23 (15) | 22 (15) | 22 (15) |
| **PAS total** | 0 | 20 (11) | 20 (11) | 20 (11) |
| **PAS (panic attacks)** | 0 | 1.07 (0.98) | 1.08 (1.00) | 1.08 (0.99) |
| **PAS (agoraphobic avoidance)** | 0 | 1.60 (1.14) | 1.55 (1.12) | 1.57 (1.13) |
| **PAS (anticipatory anxiety)** | 0 | 1.94 (1.28) | 1.94 (1.23) | 1.94 (1.26) |
| **PAS (disability)** | 0 | 1.36 (0.97) | 1.38 (0.98) | 1.37 (0.97) |
| **PAS (worries about health)** | 0 | 1.08 (1.07) | 1.17 (1.12) | 1.13 (1.10) |
| **MI (alone subscale)** | 9 | 2.30 (0.87) | 2.23 (0.85) | 2.27 (0.86) |
| **MI (accompanied subscale)** | 8 | 1.83 (0.68) | 1.72 (0.65) | 1.77 (0.67) |
| **PANAS (positive)** | 0 | 25.9 (4.1) | 26.1 (4.3) | 26.0 (4.2) |
| **PANAS (negative)** | 0 | 25.4 (4.3) | 25.7 (4.1) | 25.6 (4.2) |
| **PFBK** | 225 | 19.7 (4.9) | 20.2 (4.9) | 20.0 (4.9) |
| **QUOL** | 0 | 1.84 (1.09) | 1.81 (1.07) | 1.83 (1.08) |
| **WHODAS** | 0 | 23 (7) | 23 (7) | 23 (7) |
| **WHODAS (in %)** | 0 | 48 (16) | 49 (15) | 48 (15) |
| **WST** | 0 | 26.1 (4.7) | 26.3 (4.7) | 26.2 (4.7) |
| **ZST** | 0 | 52 (12) | 54 (13) | 53 (13) |
| **ZST (wrong answers)** | 33 | 1.20 (8.13) | 0.70 (5.80) | 0.95 (7.07) |
| **HAMA total post-treatment** | 0 | 12 (8) | 13 (9) | 13 (8) |
| *1*n (% %); Mean (SD); Median (Minimum-Maximum) |

Note. Variables are presented in the following order: sociodemographic variables, disorder-related variables, and questionnaire and behavioral variables. All diagnoses are 12-months diagnoses. Abbreviations: NA = missings, # = number, BMI = Body-Mass-Index, AAQ = acceptance and action questionnaire-II, ACQ = agoraphobic cognitions questionnaire, ASI = anxiety sensitivity index, BDI-II = Beck depression inventory-II, BSI = brief symptom inventory, BSI-GSI = BSI sum score divided by #items >0, BIS = Barratt Impulsiveness Scale [short version], BIS-BAS = Behavioral Inhibition System and Behavioral Approach System, BSQ = bodily sensations questionnaire, CGI = Clinical Global Impression, CTS = Childhood Trauma Screener, DSM-5 SP = Dimensional Specific Phobia Scale for DSM‐5, DSM-5 Cross-D = Dimensional Cross-Disorder Scale for DSM‐5, EQ5 = Health Related Quality of Life, ERQ = Emotion Regulation Questionnaire, GAD7 = Generalized Anxiety Disorder 7, HAMA = Hamilton Anxiety Scale, LSAS = Liebowitz Social Anxiety Scale, MI = mobility inventory, PANAS = positive and negative affect schedule, PAS = panic and agoraphobia scale, PFBK = partnership questionnaire, QUOL = WHO Quality of Life Questionnaire, WHODAS = World Health Organization Disability Assessment Schedule [short version], WST = Wortschatztest [German vocabulary test], ZST = Zahlen-Symbol-Test [numbers and symbols test].

# Supplement D

**Machine learning pipeline**

A fully workable script for the advanced (low bias) approach is freely available at <https://github.com/Charlotte-Marie/PAI_Advanced_Approach>. The exact hyperparameter initialization of our pipeline as well as the hyperparameter tuning can also be inspected there. As stated in the main manuscript, we conducted an additional exploratory post-hoc analysis that used a Random Forest regression instead of the ridge regression, while keeping the overall approach and all other components constant.

For the Random Forest regression, we used the following hyperparameters: n\_estimators=100, criterion= squared\_error', max\_depth=None, min\_samples\_split=5, min\_samples\_leaf=1, min\_weight\_fraction\_leaf=0.0, max\_features=1.0, max\_leaf\_nodes=None, min\_impurity\_decrease=0.0, bootstrap=True, oob\_score=False, random\_state=0, verbose=0, warm\_start=False, ccp\_alpha=0.0, max\_samples=None

**Calculation of composite scores**

For the second exploratory analysis, two composite scores were calculated as alternative outcome measures in the Protect-AD dataset:

* a symptom index, based on:
	+ HAM-A
	+ Clinical global impression scale (CGI)
	+ DSM-5 Cross-D
	+ a symptom severity questionnaire score depending on the primary diagnosis: Liebowitz Anxiety Scales (LSAS), Panic and agoraphobia scale (PAS), or Dimensional Specific Phobia Scale for DSM‐5 (DSM\_sp\_sum)
* a functioning index, based on:
	+ World Health Organization Disability Schedule (WHODAS 2.0)
	+ EuroQOL five-dimensional measure of health status (EQ-5D)
	+ global assessment of functioning (GAF).

To calculate both composite scores, single scores were brought into a similar range before being summed up by standardization based on their range. The complete procedure of generating the composite scores can be found on Github (<https://github.com/Charlotte-Marie/PAI-paper_analyses>)

# Supplement E

PAI evaluation metrics for the 50% of patients with the highest absolute PAI

| Metric | PANIC-net |  | Protect-AD | Protect-AD symptom | Protect-AD function |
| --- | --- | --- | --- | --- | --- |
| trad(linear) | adv(ridge) | adv(ridge w hp) | adv(rf) | trad(linear) | adv(ridge) | adv(ridge w hp) | adv(rf) | adv(ridge) | adv(ridge) |
| t-test 50 perc | *p* < 0.001  | 1/100 | 1/100 | 0/100 |  | *p* < 0.001 | 14/100 | 8/100 | 5/100 | 0/100 | 4/100 |
| Cohen´s d 50 perc | 0.56 | 0.01 (0.15) | -0.01 (0.15) | -0.13 (0.12) |  | 0.54 | 0.08 (0.1) | 0.05 (0.09) | 0.04 (0.09) | -0.07 (0.08) | 0.05 (0.09) |
| Mean PAI 50 perc | 3.93 | 7.27 (0.44) | 7.45 (0.5) | 4.66 (0.24) |  | 5.00 | 5.3 (0.23) | 5.52 (0.26) | 5.06 (0.19) | 1.29 (0.13) | 0.48 (0.02) |

Notes. Please note that the values given for the t-test differ for both approaches. For the traditional approach, the p-value is given. For the advanced approaches, the proportion of repetitions in which the t-tests got significant are given. All other values presented in the advanced approaches represent the mean values across 100 repetitions of 5-fold CV, accompanied by their corresponding standard deviations in brackets. In contrast, the values in the traditional approach are single values without means. Abbreviations: PAI = Personalized advantage index, MAE = mean absolute error; RMSE = root mean square error, trad = traditional, adv = advanced, linear = linear regression, ridge = ridge regression, w hp = with hyperparameter tuning, rf = random forest

# Supplement F

PAI and model performance evaluation metrics in the mixed approach

| Metric |  | PANIK-net | Protect-AD |
| --- | --- | --- | --- |
| Trad + adv(linear) | Trad + adv(linear) |
| t-test  |  | 3/100 | 9/100 |
| Cohen´s d |  | -0.026 (0.12) | 0.05 (0.06) |
| Cohen´s d 50% |  | -0.01 (0.16) | 0.07 (0.09) |
| MAE |  | 5.59 (0.62) | 6.45 (0.42) |
| RMSE |  | 7.14 (0.78) | 8.13 (0.55) |
| Correlation |  | 0.40 (0.12) | 0.31 (0.08) |