Supplementary material

# Machine learning meta-analysis identifies individual characteristics moderating cognitive intervention efficacy for anxiety and depression symptoms

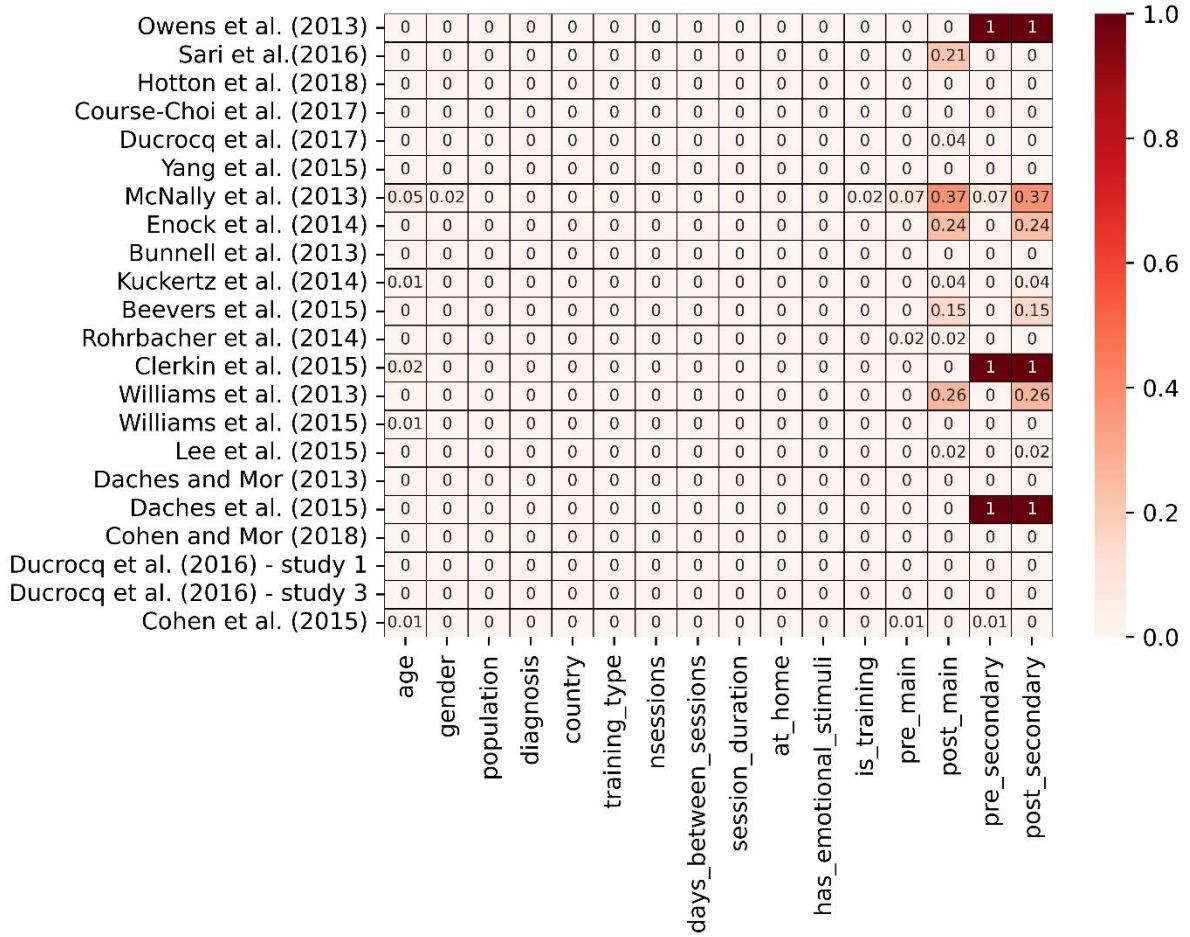
## Supplementary Information 1: Missing data

Participants assigned to a passive control condition (e.g., waiting list) were excluded from the full data set analysis to allow for the investigation of study-level moderators. This led to the removal of 78 participants. Additionally, 125 participants were missing a post-training main score, and 8 lacked demographic information, leaving a total of 1,333 participants for the analysis of Aim 1 main outcome and 1,116 participants for the secondary outcome analysis.

For Aim 2, the analysis focused on participants assigned to one of the training conditions, totaling 771 individuals. After excluding those with missing data, 694 participants remained for the main outcome analysis and 588 for the secondary outcome.

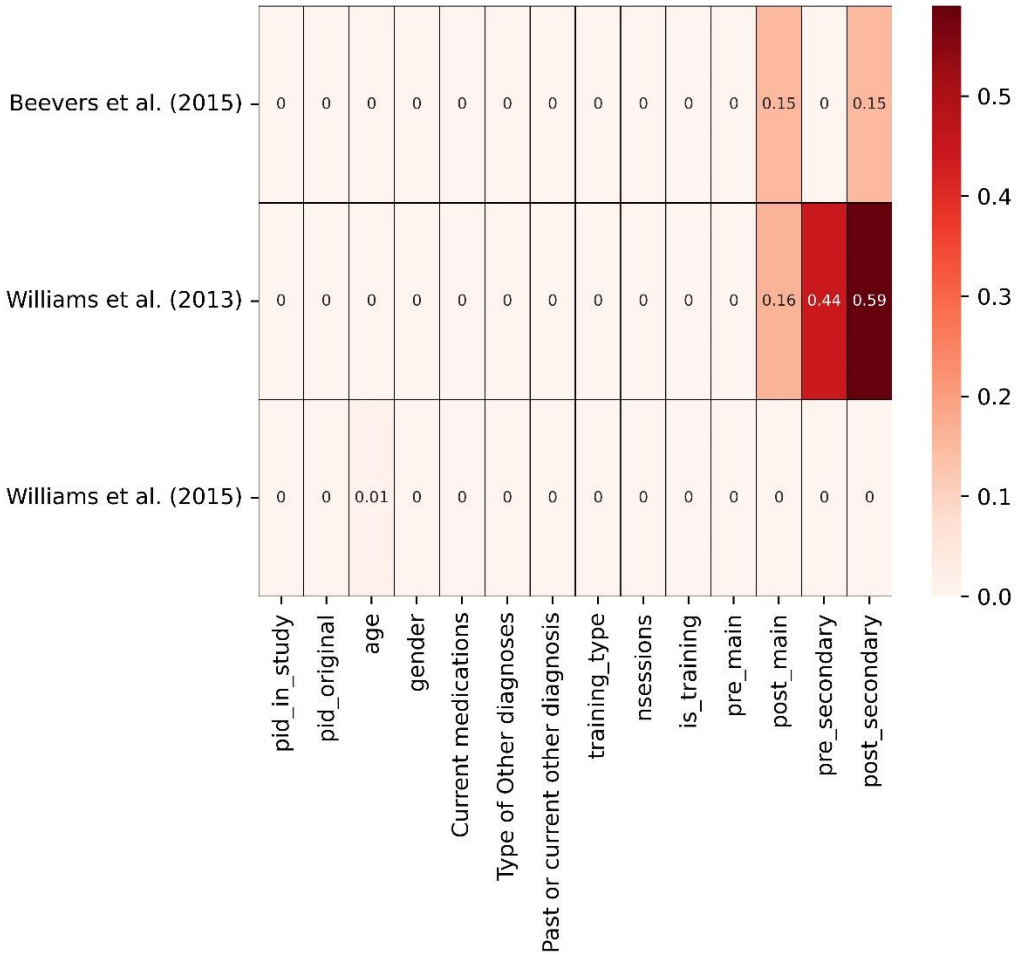
The clinical data set analysis included 190 participants across three studies. After accounting for missing data, 171 participants were included in the analysis of Aim 1 main outcome, 144 in the secondary outcome analysis, and 86 in the Aim 2 main and secondary outcome analyses.

### Supplementary Figure 1: Missing data analysis of the complete data set




Supplementary Figure 1. *Missing data analysis of the complete data set.* The figure shows the proportion of missing data for each predictor variable across the included studies. The color intensity indicates the proportion of missing values, with darker shades representing a higher proportion of missing data.

**Supplementary Figure 2: Missing data analysis of the clinical data set**




Supplementary Figure 2. *Missing data analysis of the clinical data set.* The figure shows the proportion of missing data for each predictor variable across the included studies. The color intensity indicates the proportion of missing values, with darker shades representing a higher proportion of missing data

**Supplementary Table 1, 2, & 3: Results of the LME analysis of the complete data set**

Table 1 presents MSE values of the training and validation sets for the main and secondary outcomes.

Supplementary Table 1. *MSE values for the main and secondary outcomes prediction of Aim 1.*

| | **Training MSE** | **Validation MSE** |
|---|---|---|
| Main outcome | 1.23 | 0.99 |
| Secondary outcome | 0.46 | 0.44 |

Similarly to the MSE values of the RF model, the MSE values for the LME model demonstrate relatively high accuracy, with values falling within less than one standard deviation of the standardized outcome scale.

Tables 2 and 3 present the individual and study-level moderators selected for the model through backward-stepwise regression based on AIC, along with their Beta coefficients and the Beta coefficients of the interactions between the moderators.

Supplementary Table 2. *Beta coefficients of Aim 1: Main outcome*

| | | Gain main | |
|---|---|---|---|
| ***Predictors*** | ***Estimates*** | ***CI*** | ***p*** |
| (Intercept) | -0.25 | -0.88– 0.38 | 0.438 |
| is training [2] | -0.15 | -0.66 – 0.35 | 0.552 |
| nsessions | 0.01 | 0.01 – 0.02 | **0.001** |
| days between sessions | 0.11 | -0.03 – 0.25 | 0.115 |
| session duration | -0.02 | -0.03 – -0.00 | **0.030** |
| at home [2] | 0.42 | 0.03 – 0.81 | **0.033** |
| has emotional stimuli [2] | 0.52 | 0.20 – 0.83 | **0.001** |
| country [2] | -0.11 | -0.50 – 0.28 | 0.587 |
| diagnosis [2] | -0.02 | -0.48 – 0.44 | 0.942 |
| pre main | 0.35 | 0.20 – 0.49 | **<0.001** |
| is training [2] X days between sessions | -0.18 | -0.35 – -0.01 | **0.042** |
| is training [2] X at home [2] | -0.41 | -0.77 – -0.05 | **0.024** |
| is training [2] X diagnosis [2] | 0.45 | 0.03 – 0.87 | **0.035** |
| is training [2] X pre main | -0.12 | -0.21 – -0.03 | **0.008** |
| days between sessions X pre main | -0.10 | -0.14 – -0.07 | **<0.001** |
| at home [2] X pre main | 0.27 | 0.18 – 0.37 | **<0.001** |
| has emotional stimuli [2] X pre main | 0.18 | 0.06 – 0.29 | **0.002** |
| country [2] X pre main | 0.14 | 0.03 – 0.26 | **0.015** |
| diagnosis [2] X pre main | -0.30 | -0.43 – -0.17 | **<0.001** |
| (is training [2] X days between sessions) X pre main | 0.14 | 0.09 – 0.19 | **<0.001** |
| **Random Effects** | | | |
| $\sigma^2$ | 1.26 | | |
| $\tau_{00}$ study | 0.00 | | |
| N study | 22 | | |
| Observations | 928 | | |
| Marginal $R^2$ / Conditional $R^2$ | 0.367 / NA | | |

Supplementary Table 3. *Beta coefficients of Aim 1: Secondary outcome.*

| | | **Gain secondary** | |
|---|---|---|---|
| ***Predictors*** | ***Estimates*** | ***CI*** | ***p*** |
| (Intercept) | 0.46 | -0.55– 1.48 | 0.370 |
| is training [2] | -0.50 | -0.78 – -0.21 | **0.001** |
| nsessions | 0.00 | -0.01 – 0.01 | 0.991 |
| days between sessions | 0.02 | -0.16 – 0.19 | 0.853 |
| session duration | -0.02 | -0.05 – 0.00 | 0.053 |
| population [2] | -0.20 | -0.60 – 0.19 | 0.314 |
| population [3] | 0.30 | -0.16 – 0.76 | 0.203 |
| age | -0.00 | -0.01 – 0.00 | 0.208 |
| gender [1] | -0.91 | -1.53 – -0.28 | **0.004** |
| pre secondary | 0.26 | 0.15 – 0.38 | **<0.001** |
| is training [2] X age | 0.02 | 0.01 – 0.03 | **0.001** |
| is training [2] X pre secondary | -0.11 | -0.19 – -0.02 | **0.011** |
| nsessions X gender [1] | 0.01 | 0.00 – 0.02 | **0.009** |
| days between sessions X gender [1] | 0.15 | 0.04 – 0.27 | **0.010** |
| Session duration X gender [1] | 0.03 | 0.01 – 0.04 | **0.007** |
| population [2] X pre secondary | 0.27 | 0.13 – 0.41 | **<0.001** |
| population [3] X pre secondary | 0.09 | -0.06 – 0.23 | 0.251 |
| **Random Effects** | | | |
| $\sigma^2$ | 0.47 | | |
| $\tau_{00}$ study | 0.06 | | |
| ICC | 0.11 | | |
| N study | 19 | | |
| Observations | 778 | | |
| Marginal $R^2$ / Conditional $R^2$ | 0.341/ 0.415 | | |

# PRISMA 2020 Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | -Title<br>-Shani et al. [8]: Title |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | -Abstract<br>-Shani et al. [8]: Abstract |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | -Introduction<br>-Shani et al. [8]: Introduction |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | -Introduction<br>-Shani et al. [8]: Introduction |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Shani et al. [8]: Methods |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Shani et al. [8]: Methods |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Shani et al. [8]: Methods |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Shani et al. [8]: Methods |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Shani et al. [8]: Methods |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Shani et al. [8]: Methods |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Shani et al. [8]: Methods |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Shani et al. [8]: Methods and Supplementary Material |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | -Methods.<br>-Shani et al. [8]: Methods |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | -Methods.<br>-Shani et al. [8]: Methods |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | -Methods.<br>-Shani et al. [8]: Methods |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Methods |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Methods |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Methods |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Methods |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Supplementary Figure 1 and Supplementary Figure 2 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Methods |
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Shani et al. [8]: Methods |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Shani et al. [8]: Methods and Supplementary Material |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Shani et al. [8]: Methods |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Shani et al. [8]: Supplementary Material |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Not Applicable |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Shani et al. [8]: Supplementary Material |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Results |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Results |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Results |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Supplementary Figure 1 and Supplementary Figure 2 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Results |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Discussion |
| | 23b | Discuss any limitations of the evidence included in the review. | Discussion |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | 23c | Discuss any limitations of the review processes used. | Discussion |
| | 23d | Discuss implications of the results for practice, policy, and future research. | Discussion |
| **OTHER INFORMATION** | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Methods |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Methods |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | Methods |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Acknowledgments |
| Competing interests | 26 | Declare any competing interests of review authors. | Competing Interests Statement |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Data and Code Availability Statements |

*From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71