**Supplement 1**

**e-Table 1.** Outline of the Danish Group UP Protocol Session-to-session and Corresponding UP modules

**e-Fig. 1.** Mean Differences and 2-sided 95% Confidence Intervals for the WHO-5 Well-being Index and Non-inferiority Margin

**e-Table 2.** Means, Estimated Mean Differences, and Between-condition Effect Sizes for Diagnosis-specific Outcomes

**e-Table 3.** Imputed Mean scores and Unadjusted Within-condition Effect Sizes for Primary and Secondary Outcomes

**e-Table 4.** Imputed Means and Unadjusted Within-condition Effect Sizes for Diagnosis-specific Outcomes

**e-Table 5.** Type and Number of Reported Adverse Events for the Intention-to-treat Population

|  |  |
| --- | --- |
| **Session** | **UP Module** |
| Pre-group session |  |
| 1 | Motivation Enhancement for Treatment Engagement |
| 2 | Psychoeducation and Tracking of Emotional Experiences |
| 3 | Emotion Awareness Training |
| 4 | Cognitive Appraisal and Reappraisal |
| 5 | Emotion Avoidance and Emotion-driven Behaviors |
| 6 | Awareness and Tolerance of Physical Sensations |
| 7-13 | Interoceptive and Situation-based Emotion Exposures |
| 14 | Relapse Prevention |

**e-Table 1.** Outline of the Danish Group UP Version Session-to-session and Corresponding UP modules

Abbreviations: UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders

**e-Fig. 1.** Mean Differences and 2-sided 95% Confidence Intervals for the WHO-5 and Non-inferiority Margin

Abbreviations: UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders; dCBT, Diagnosis-specific Cognitive-behavioral Therapy; WHO-5, World Health Organization Five Well-being Index.

Non-inferiority of UP compared to dCBT at end-of-treatment. The estimated between-condition mean difference was -2.94 (95% CI, -8.10 to 2.21; *P*=0.26) WHO-5 scale points favoring dCBT. We accepted non-inferiority of UP to dCBT as the lower limit of the 95% CI was within the *a priori* non-inferiority limit of ∆ =9 WHO-5 scale points.

Non-inferiority of UP compared to dCBT at 6-month follow-up. The estimated between-condition mean difference was -6.42 (95% CI, -12.31 to -0.53; *P*=0.03) WHO-5 points favoring dCBT, indicating possible inferiority of UP to dCBT. The result was inconclusive whether this difference is clinically meaningful as the 95% CI included the non-inferiority limit ∆ =9 WHO-5 scale points.

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|  | **Mean (95%CI)** | | | | **Adjusted Effect Estimates a** | | |
| **Outcome and Assessment** | **n =** | **UP** | **n =** | **dCBT** | **Mean Difference b**  **(95% CI)** | ***P***  **Value** | **Cohen’s *d***  **(95%CI)** |
| **Depression Outcomes** |  |  |  |  |  |  |  |
| Beck Depression Inventory-II | | |  |  |  |  |  |
| Baseline c | 42 | 29.29 (27.06 to 31.51) | 45 | 29.93 (27.45 to 32.42) | NA | NA | NA |
| End-of-treatment | 48 | 22.50 (19.56 to 25.44) | 50 | 20.91 (18.05 to 23.78) | 1.59 (-2.40 to 5.58) | 0.44 | 0.15 (-0.23 to 0.54) |
| 6-month Follow-up | 48 | 21.67 (18.34 to 24.99) | 50 | 19.04 (15.76 to 22.33) | 2.62 (-2.06 to 7.31) | 0.27 | 0.23 (-0.18 to 0.63) |
| Hamilton Depression Rating Scale-6 items | | |  |  |  |  |  |
| Baseline | 48 | 8.98 (7.90 to 10.06) | 48 | 9.17 (8.14 to 10.20) | NA | NA | NA |
| End-of-treatment | 48 | 6.67 (5.50 to 7.84) | 50 | 6.95 (5.78 to 8.12) | -0.28 (-1.85 to 1.30) | 0.73 | -0.07 (-0.44 to 0.31) |
| 6-month Follow-up | 48 | 6.02 (4.81 to 7.23) | 50 | 6.20 (4.96 to 7.44) | -0.18 (-1.90 to 1.54) | 0.84 | -0.04 (-0.44 to 0.36) |
| **Anxiety Outcomes** |  |  |  |  |  |  |  |
| Hamilton Anxiety Rating Scale-6 items | | |  |  |  |  |  |
| Baseline | 48 | 9.90 (8.73 to 11.07) | 42 | 8.88 (7.46 to 10.30) | NA | NA | NA |
| End-of-treatment | 50 | 6.89 (5.53 to 8.26) | 43 | 7.73 (6.21 to 9.25) | -0.84 (-2.80 to 1.13) | 0.40 | -0.17 (-0.56 to 0.23) |
| 6-month Follow-up | 50 | 6.48 (5.21 to 7.74) | 43 | 5.13 (3.72 to 6.55) | 1.35 (-0.57 to 3.26) | 0.17 | 0.29 (-0.12 to 0.71) |
| Liebowitz Social Anxiety Scale | | |  |  |  |  |  |
| Baseline | 19 | 93.14 (81.02 to 105.27) | 13 | 77.77 (64.45 to 91.09) | NA | NA | NA |
| End-of-treatment | 30 | 64.79 (54.78 to 74.80) | 21 | 63.83 (49.84 to 77.81) | 0.96 (-15.97 to 17.90) | 0.91 | 0.03 (-0.53 to 0.60) |
| 6-month Follow-up | 30 | 62.42 (49.84 to 75.00) | 21 | 66.49 (52.17 to 80.81) | -4.07 (-24.88 to 16.75) | 0.69 | -0.12 (-0.75 to 0.50) |
| Panic Disorder Severity Scale | | |  |  |  |  |  |
| Baseline | 20 | 15.55 (13.47 to 17.67) | 21 | 13.86 (10.97 to 16.75) | NA | NA | NA |
| End-of-treatment | 20 | 10.23 (6.99 to 13.46) | 22 | 9.20 (5.99 to 12.41) | 0.55 (-3.74 to 4.85) | 0.79 | 0.07 (-0.50 to 0.65) |
| 6-month Follow-up | 20 | 10.01 (6.60 to 13.41) | 22 | 5.39 (2.08 to 8.70) | 4.62 (-0.11 to 9.35) | 0.06 | 0.62 (-0.02 to 1.26) |
| Mobility Inventory (Avoidance Subscale) | | |  |  |  |  |  |
| Baseline | 20 | 3.30 (2.81 to 3.73) | 21 | 2.60 (2.07 to 3.11) | NA | NA | NA |
| End-of-treatment | 20 | 2.61 (2.20 to 3.03) | 22 | 2.41 (2.04 to 2.78) | 0.20 (-0.32 to 0.72) | 0.44 | 0.22 (-0.35 to 0.79) |
| 6-month Follow-up | 20 | 2.55 (1.99 to 3.11) | 22 | 1.89 (1.34 to 2.44) | 0.66 (-0.15 to 1.46) | 0.10 | 0.54 (-0.12 to 1.20) |

**e-Table 2.** Means, Estimated Mean Differences, and Between-condition Effect Sizes for Diagnosis-specific Outcomes

Abbreviations: UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders; dCBT, Diagnosis-specific Cognitive-behavioral therapy; NA, not applicable.

a ANCOVA-tests adjustment: stratification variables (principal diagnosis, treatment site) and baseline scores.

b Negative scores and effect sizes indicate that dCBT had higher scores at follow-up. Positive scores and effect sizes indicate that dCBT had lower scores at follow-up. Lower scores are better for all outcomes.

c Baseline scores are observed data. Follow-up data are based on adjusted ANCOVA-tests (baseline scores and stratification variables) on imputed data.

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|  |  | **Mean Scores (95% CI)** | | | **Unadjusted Effect Sizes, Cohen’s *d* (95% CI) a** | |
| **Outcome and Condition** | **N=** | **Baseline** | **End-of-treatment** | **6-month Follow-up** | **Baseline to**  **End-of-treatment** | **Baseline to**  **6-month Follow-up** |
| **Primary Outcome** |  |  |  |  |  |  |
| WHO-5 Well-being Index |  |  |  |  |  |  |
| UP | 98 | 31.46 (27.88 to 35.03) | 42.44 (37.85 to 47.02) | 45.72 (40.92 to 50.53) | 0.53 (0.33 to 0.73) | 0.67 (0.43 to 0.90) |
| dCBT | 93 | 29.76 (25.78 to 33.75) | 44.19 (39.28 to 49.10) | 51.32 (46.23 to 56.34) | 0.66 (0.41 to 0.90) | 0.96 (0.68 to 1.25) |
| **Secondary Outcomes** |  |  |  |  |  |  |
| Symptom Check List-25 Items |  |  |  |  |  |  |
| UP | 98 | 2.0 (1.86 to 2.13) | 1.59 (1.43 to 1.75) | 1.43 (1.28 to 1.59) | -0.54 (-0.74 to -0.34) | -0.76 (-0.99 to -0.54) |
| dCBT | 93 | 2.0 (1.85 to 2.14) | 1.49 (1.33 to 1.66) | 1.30 (1.13 to 1.47) | -0.65 (-0.86 to -0.44) | -0.89 (-1.13 to -0.64) |
| Hamilton Depression Rating Scale-6 Items | | |  |  |  |  |
| UP | 98 | 8.51 (7.78 to 9.24) | 6.55 (5.79 to 7.31) | 5.89 (5.05 to 6.73) | -0.52 (-0.75 to -0.29) | -0.66 (-0.91 to -0.42) |
| dCBT | 93 | 8.56 (7.80 to 9.32) | 6.86 (5.87 to 7.85) | 5.73 (4.78 to 6.68) | -0.39 (-0.62 to -0.16) | -0.67 (-0.92 to -0.42) |
| Hamilton Anxiety Rating Scale-6 Items | | |  |  |  |  |
| UP | 98 | 8.98 (8.13 to 9.83) | 6.36 (5.43 to 7.30) | 6.03 (5.13 to 6.93) | -0.58 (-0.80 to -0.36) | -0.67 (-0.90 to -0.44) |
| dCBT | 93 | 7.97 (7.10 to 8.84) | 6.79 (5.88 to 7.71) | 4.92 (3.92 to 5.92) | -0.27 (-0.50 to -0.04) | -0.66 (-0.91 to -0.41) |
| Work and Social Adjustment Scale | | |  |  |  |  |
| UP | 98 | 24.64 (23.26 to 26.06) | 20.06 (18.31 to 21.81) | 16.97 (14.87 to 19.08) | -0.57 (-0.79 to -0.35) | -0.85 (-1.07 to -0.62) |
| dCBT | 93 | 26.07 (24.39 to 27.75) | 19.41 (17.29 to 21.54) | 16.38 (14.01 to 18.75) | -0.71 (-0.92 to -0.49) | -0.96 (-1.20 to -0.72) |

**e-Table 3.** Imputed Mean scores and Unadjusted Within-condition Effect Sizes for Primary and Secondary Outcomes

Abbreviations: UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders; dCBT, Diagnosis-specific Cognitive-behavioral Therapy; WHO-5, World Health Organization Five Well-being Index.

a Negative effect sizes mean that follow-up scores were lower than baseline scores. Positive effect sizes are better for the primary outcome. Negative effect sizes are better for the secondary outcomes.

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|  |  | **Mean scores (95% CI)** | | | **Unadjusted Effect Sizes, Cohen’s *d* (95% CI) a** | |
| **Outcome and Condition** | **N=** | **Baseline** | **End-of-treatment** | **6-month Follow-up** | **Baseline to**  **End-of-treatment** | **Baseline to**  **6-month Follow-up** |
| **Depression Outcomes** |  |  |  |  |  |  |
| Beck Depression Inventory-II |  |  |  |  |  |  |
| UP | 48 | 29.80 (27.60 to 32.01) | 22.43 (19.31 to 25.55) | 21.43 (17.94 to 24.92) | -0.77 (-1.09 to -0.46) | -0.81 (-1.15 to -0.48) |
| dCBT | 50 | 29.80 (27.41 to 32.19) | 21.88 (18.48 to 25.27) | 19.27 (15.46 to 23.08) | -0.75 (-1.06 to -0.44) | -0.92 (-1.24 to -0.60) |
| Hamilton Depression Rating Scale-6 | | |  |  |  |  |
| UP | 48 | 8.98 (7.93 to 10.03) | 6.68 (5.61 to 7.75) | 5.95 (4.80 to 7.10) | -0.61 (-0.94 to -0.29) | -0.78 (-1.13 to -0.43) |
| dCBT | 50 | 9.12 (8.12 to 10.13) | 7.23 (5.88 to 8.60) | 6.27 (4.90 to 7.64) | -0.44 (-0.74 to -0.14) | -0.66 (-1.0 to -0.32) |
| **Anxiety Outcomes** |  |  |  |  |  |  |
| Hamilton Anxiety Rating Scale-6 | |  |  |  |  |  |
| UP | 50 | 9.75 (8.59 to 10.91) | 6.90 (5.42 to 8.40) | 6.71 (5.30 to 8.12) | -0.59 (-0.92 to -0.27) | -0.65 (-0.99 to -0.32) |
| dCBT | 43 | 8.83 (7.45 to 10.21) | 7.17 (5.77 to 8.57) | 4.86 (3.44 to 6.28) | -0.40 (-0.72 to 0.00) | -0.85 (-1.21 to -0.49) |
| Liebowitz Social Anxiety Scale |  |  |  |  |  |  |
| UP | 30 | 93.59 (82.43 to 104.75) | 72.40 (60.44 to 84.36) | 65.54 (52.50 to 78.58) | -0.66 (-0.99 to -0.32) | -0.83 (-1.22 to -0.43) |
| dCBT | 21 | 74.69 (61.10 to 88.32) | 66.48 (56.14 to 76.83) | 62.03 (50.24 to 73.82) | -0.29 (-0.79 to 0.21) | -0.43 (-1.03 to 0.18) |
| Panic Disorder Severity Scale |  |  |  |  |  |  |
| UP | 20 | 15.55 (13.60 to 17.50) | 9.71 (6.70 to 12.73) | 10.40 (7.03 to 13.78) | -1.01 (-1.63 to -0.39) | -0.82 (-1.39 to -0.25) |
| dCBT | 22 | 13.68 (10.90 to 16.46) | 8.10 (4.65 to 11.55) | 5.03 (1.70 to 8.35) | -0.74 (-1.16 to -0.33) | -1.18 (-1.76 to -0.60) |
| Mobility Inventory (Avoidance Subscale) | | |  |  |  |  |
| UP | 20 | 3.30 (2.90 to 3.70) | 2.73 (2.24 to 3.23) | 2.80 (2.20 to 3.35) | -0.55 (-0.91 to -0.19) | -0.47 (-0.86 to -0.07) |
| dCBT | 22 | 2.59 (2.08 to 3.09) | 2.05 (1.53 to 2.57) | 1.68 (1.10 to 2.28) | -0.44 (-0.78 to -0.10) | -0.69 (-1.13 to -0.25) |

**e-Table 4.** Imputed Means and Unadjusted Within-condition Effect Sizes for Diagnosis-specific Outcomes

Abbreviations: UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders; dCBT, Diagnosis-specific Cognitive-behavioral Therapy.

a Negative effect sizes mean that follow-up scores were lower than baseline scores. Negative effect sizes are better for all outcomes.

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| --- | --- | --- | --- |
|  | **No. Adverse Events** | | |
| **Type of Adverse Event** | **UP** | **dCBT** | **Total** |
| **Minor Adverse Events** |  |  |  |
| Increasing current medication > 1 standard dose step | 6 | 4 | 10 |
| Using according-to-need medication for > 2 weeks | 7 | 6 | 13 |
| Increasing current medication to entail > 4 types of psychotropic medication | 2 | 3 | 5 |
| New prescription of supplementary medication (accepted at inclusion) | 12 | 13 | 25 |
| Changing previously prescribed antidepressant to another type (accepted at inclusion) | 8 | 10 | 18 |
| **Total** | **35** | **36** | **71** |
| **Major Adverse Events** |  |  |  |
| New prescription of medication (not accepted at inclusion) | 6 | 10 | 16 |
| Contacting psychiatric emergency due to self-injury | 8 | 6 | 14 |
| Suicide attempt without hospitalization | 1 | - a | 1 |
| Drop-out of therapy due to experienced lack of effect or deterioration | 5 | 6 | 11 |
| **Total** | **20** | **22** | **41** |
| **Critical Adverse Events** |  |  |  |
| Psychiatric hospitalization due to deterioration or suicide attempt | 2 | - | 2 |
| Somatic hospitalization due to self-injury or suicide attempt | - | - | - |
| Suicide | - | - | - |
| **Total** | **2** | **-** | **2** |
| **Total Adverse Events** | **56** | **58** | **114** |

**e-Table 5.** Type and Number of Reported Adverse Events for the Intention-to-treat Population

Abbreviations: UP, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders; dCBT, Diagnosis-specific Cognitive-behavioral Therapy.

a – indicates no reported adverse events.