Supplemental Digital Content 2 to

**Internet-based cognitive-behavioral writing therapy for reducing posttraumatic stress after severe sepsis in patients and their spouses (REPAIR): results of a randomized controlled trial**

Romina Gawlytta; Miriam Kesselmeier; André Scherag; Helen Niemeyer; Maria Boettche; Christine Knaevelsrud, Jenny Rosendahl

**Supplemental tables**

List of tables

[**Table S1.** Characteristics of participants - stratified by post-ICU patient/spouse status and by treatment group. 2](#_Toc50361757)

[**Table S2.** Outcomes of participants - overall as well as stratified by treatment group. 4](#_Toc50361758)

[**Table S3.** Outcomes of participants - overall as well as stratified by post-ICU patient/spouse status and by treatment group. 6](#_Toc50361759)

[**Table S4.** Results for PCL-5 (PTSD Checklist for DSM-5) change from generalized estimating equation (GEE) modelling. 9](#_Toc50361760)

[**Table S5.** Results for RAS (Relationship Satisfaction Scale) change from generalized estimating equation (GEE) modelling. 10](#_Toc50361761)

[**Table S6.** Results for remission from generalized estimating equation (GEE) modelling. 11](#_Toc50361762)

[**Table S7.** Results for BSI-18 (Brief Symptom Inventory-18) change from generalized estimating equation (GEE) modelling. 12](#_Toc50361763)

[**Table S8.** Results for EQ-5D-5L (Health questionnaire of the EuroQol group in five dimensions with five levels) change in utility values from generalized estimating equation (GEE) modelling. 13](#_Toc50361764)

[**Table S9.** Between-group effect sizes (Cohen´s d, standardized mean differences) for pre-post changes in primary and secondary outcomes 15](#_Toc50361765)

[**Table S10.** Overview about safety variables - overall as well as stratified by treatment group. 16](#_Toc50361766)

[**Table S11.** Overview about safety variables - overall as well as stratified by post-ICU patient/spouse status and by treatment group. 17](#_Toc50361767)

[**Table S12.** Dyadic concordance in treatment effects in terms of PCL-5 (PTSD Checklist for DSM-5) change. 18](#_Toc50361768)

**Table S1.** Characteristics of participants - stratified by post-ICU patient/spouse status and by treatment group.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Characteristic | Post-ICU patient | | | Spouse | | |
| Overall | Treatment group | | Overall | Treatment group | |
| iCBT | WL control | iCBT | WL control |
| Male sex; *n* (%) | 17 (68.0) | 7 (58.3) | 10 (76.9) | 9 (36.0) | 5 (41.7) | 4 (30.8) |
| Age, in years; median (Q1, Q3) | 56 (48, 65) | 57 (54, 67) | 55 (46, 59) | 54 (47, 61) | 55 (51, 63) | 53 (46, 58) |
| Among post-ICU patients |  |  |  |  |  |  |
| Time since ICU treatment, in years; median (Q1, Q3) | 1.8 (1.1, 3.7) | 1.9 (1.2, 4.6) | 1.6 (1.0, 2.0) | - | - | - |
| Duration of ICU treatment, in days; median (Q1, Q3) | 21 (13, 40) | 28 (12, 42) | 21 (13, 28) | - | - | - |
| Mechanical ventilation |  |  |  |  |  |  |
| Yes; *n* (%) | 18 (72.0) | 9 (75.0) | 9 (69.2) | - | - | - |
| No; *n* (%) | 5 (20.0) | 2 (16.7) | 3 (23.1) | - | - | - |
| Not specified; *n* (%) | 2 (8.0) | 1 (8.3) | 1 (7.7) | - | - | - |
| Duration of mechanical ventilation among ventilated patients, in days; median (Q1, Q3)\*\* | 24 (16, 28) | 28 (28, 35) | 18 (8, 23) | - | - | - |
| College or university degree; *n* (%) | 7 (28.0) | 2 (16.7) | 5 (38.5) | 10 (40.0) | 5 (41.7) | 5 (38.5) |
| Pre-existing mental disorder (prior to sepsis); *n* (%) | 9 (36.0) | 5 (41.7) | 4 (30.8) | 7 (28.0) | 4 (33.3) | 3 (23.1) |
| Treatment of pre-existing mental disorder |  |  |  |  |  |  |
| Prior to sepsis; *n* (%) | 8 (32.0) | 4 (33.3) | 4 (30.8) | 7 (28.0) | 4 (33.3) | 3 (23.1) |
| Post sepsis; *n* (%) | 4 (16.0) | 3 (25.0) | 1 (7.7) | 2 (8.0) | 1 (8.3) | 1 (7.7) |
| Presumptive PTSD diagnosis |  |  |  |  |  |  |
| Only one member of the dyad; *n* (%) | 12 (48.0) | 6 (50.0) | 6 (46.2) | 4 (16.0) | 2 (16.7) | 2 (15.4) |
| Both dyad members; *n* (%)\* | 9 (36.0) | 4 (33.3) | 5 (38.5) | 9 (36.0) | 4 (33.3) | 5 (38.5) |
| Relationship |  |  |  |  |  |  |
| Duration, in years; median (Q1, Q3)\* | 22.2  (16.2, 32.9) | 24.5  (19.1, 34.6) | 21.8  (12.5, 29.4) | 22.2  (16.2, 32.9) | 24.5  (19.1, 34.6) | 21.8  (12.5, 29.4) |
| Marital status: married; *n* (%)\* | 21 (84.0) | 10 (83.3) | 11 (84.6) | 21 (84.0) | 10 (83.3) | 11 (84.6) |

The numbers are based on the dyad population. Overall, there are 25 dyads - 12 dyads in the iCBT group and 13 dyads in the WL control group. Note that each dyad comprises one post-ICU patient and one spouse. Characteristics are summarized as median with first and third quartile (Q1, Q3) or as absolute (*n*) and relative frequency (%). Abbreviations: -, not applicable; iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; PTSD, post-traumatic stress disorder; WL, waitlist.

\* Percentage refers to dyad; \*\* missing for 9 patients (iCBT group: 6, WL control group: 3)

**Table S2.** Outcomes of participants - overall as well as stratified by treatment group.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Outcome | # participants with  missing values | Overall  (n=34) | Treatment group | |
| iCBT  (n=16) | WL control  (n=18) |
| PCL-5a; median (Q1, Q3) |  |  |  |  |
| Change from t0 to t1 | 5 | 5 (1, 10) | 6 (4, 10) | 4 (-1, 10) |
| Screening | 0 | 38 (36, 47) | 39 (36, 49) | 38 (36, 45) |
| t0 | 1 | 36 (26, 45) | 36 (26, 41) | 37 (28, 45) |
| t1 | 5 | 31 (18, 43) | 22 (16, 39) | 32 (20, 44) |
| t1+ | 4 | - | - | 20 (12, 28) |
| BSI-18b; median (Q1, Q3) |  |  |  |  |
| Change from t0 to t1 | 5 | 1 (-3, 4) | 3 (-1, 5) | -1 (-3, 4) |
| t0 | 1 | 19 (12, 25) | 19 (14, 24) | 20 (11, 25) |
| t1 | 5 | 17 (9, 28) | 13 (9, 21) | 20 (10, 28) |
| t1+ | 4 | - | - | 12 (7, 18) |
| RASc; median (Q1, Q3) |  |  |  |  |
| Change from t0 to t1 | 5 | 0 (0, 0) | 0 (0, 1) | 0 (-1, 0) |
| t0 | 1 | 2 (2, 4) | 2 (2, 4) | 2 (2, 2) |
| t1 | 5 | 2 (1, 3) | 1 (1, 4) | 2 (2, 3) |
| t1+ | 4 | - | - | 2 (1, 3) |
| EQ-5D-5Ld; median (Q1, Q3) |  |  |  |  |
| Change from t0 to t1 | 5 | 0.01 (-0.05, 0.09) | 0.01 (-0.05, 0.06) | 0.01 (-0.05, 0.14) |
| t0 | 1 | 0.69 (0.48, 0.82) | 0.73 (0.49, 0.84) | 0.66 (0.49, 0.82) |
| t1 | 5 | 0.66 (0.32, 0.83) | 0.80 (0.55, 0.85) | 0.66 (0.31, 0.82) |
| t1+ | 4 | - | - | 0.79 (0.68, 0.90) |
| PTSD; *n* (%) |  |  |  |  |
| t0 | 0 | 25 (73.5%) | 14 (87.5%) | 11 (61.1%) |
| t1 | 5 | 13 (44.8%) | 1 (9.1%) | 12 (66.7%) |
| Remission from t0 to t1\* | 4 | 12 (57.1%) | 9 (90.0%) | 3 (27.3%) |

Overall, there are 25 dyads - 12 dyads in the iCBT group and 13 dyads in the WL control group. Note that each dyad comprises one patient and one spouse. Outcomes are summarized as median with first and third quartile (Q1, Q3) or as absolute (*n*) and relative frequency (%). Percentages refer to number of participants with information for the respective value; number of participants with missing values are provided. Values are provided for several time points: t0, start of intervention (iCBT group) / waiting (WL control group); t1, end of intervention (iCBT group) / waiting (WL control group); t1+, end of intervention in WL control group. Abbreviations: -, not applicable; #, number of; BSI-18, Brief Symptom Inventory-18; CAPS-5, Clinician-Administered PTSD Scale for DSM-5; EQ-5D-5L, Health questionnaire of the EuroQol group in five dimensions with five levels; iCBT, internet-based cognitive-behavioral writing therapy; PCL-5, PTSD Checklist for DSM-5; PTSD, post-traumatic stress disorder; RAS, Relationship Satisfaction Scale; WL, waitlist.

\* Both percentage and number of missing values refer to number of participants with PTSD at t0.

a Total scores of the PCL-5 range from 0 to 80 (higher scores indicate greater severity of PTSD symptoms). PCL-5 was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

b Total scores of BSI-18 range from 0 to 72 (higher scores indicate greater severity of symptoms). BSI-18 was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

c RAS mean scores range from 1 to 7 (higher scores represent higher relationship satisfaction). RAS was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

d Total scores of EQ-5D-5L range from -0,661 to 1 (lower scores indicating worse quality of life), anchored at 0 (death) and 1 (perfect health). EQ-5D-5L was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

**Table S3.** Outcomes of participants - overall as well as stratified by post-ICU patient/spouse status and by treatment group.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Outcome | # participants with  missing values | Post-ICU patient | | | Spouse | | |
| Overall  (n=21) | Treatment group | | Overall  (n=13) | Treatment group | |
| iCBT  (n=10) | WL control  (n=11) | iCBT  (n=6) | WL control  (n=7) |
| PCL-5a; median (Q1, Q3) |  |  |  |  |  |  |  |
| Change from t0 to t1 | 5 | 8 (5, 11) | 8 (6, 12) | 8 (4, 10) | 2 (-2, 5) | 5 (4, 5) | -2 (-4, 2) |
| Screening | 0 | 38 (37, 51) | 40 (36, 51) | 38 (37, 48) | 38 (35, 41) | 39 (36, 40) | 36 (35, 43) |
| t0 | 1 | 42 (31, 50) | 37 (29, 42) | 45 (36, 51) | 26 (23, 33) | 26 (24, 36) | 29 (21, 32) |
| t1 | 5 | 36 (21, 44) | 34 (19, 40) | 36 (24, 44) | 21 (18, 33) | 21 (16, 22) | 21 (18, 35) |
| t1+ | 4 | - | - | 24 (17, 28) | - | - | 12 (11, 12) |
| BSI-18b; median (Q1, Q3) |  |  |  |  |  |  |  |
| Change from t0 to t1 | 5 | 3 (-2, 5) | 4 (3, 8) | 0 (-2, 4) | -1 (-3, 2) | 1 (-3, 2) | -1 (-8, 2) |
| t0 | 1 | 22 (16, 28) | 22 (16, 24) | 23 (14, 30) | 15 (11, 22) | 14 (12, 18) | 18 (8, 22) |
| t1 | 5 | 19 (10, 27) | 14 (10, 23) | 21 (14, 28) | 12 (8, 28) | 9 (9, 17) | 13 (9, 29) |
| t1+ | 4 | - | - | 16 (10, 20) | - | - | 7 (4, 7) |
| RASc; median (Q1, Q3) |  |  |  |  |  |  |  |
| Change from t0 to t1 | 5 | 0 (0, 1) | 1 (1, 1) | 0 (-1, 0) | 0 (0, 0) | 0 (0, 0) | 0 (0, 0) |
| t0 | 1 | 2 (2, 3) | 2 (2, 4) | 2 (2, 2) | 2 (2, 4) | 3 (2, 4) | 2 (2, 2) |
| t1 | 5 | 2 (1, 3) | 1 (1, 2) | 2 (1, 3) | 2 (2, 4) | 4 (1, 4) | 2 (2, 3) |
| t1+ | 4 | - | - | 2 (2, 2) | - | - | 2 (1, 3) |
| EQ-5D-5Ld; median (Q1, Q3) |  |  |  |  |  |  |  |
| Change from t0 to t1 | 5 | 0.00  (-0.07, 0.09) | -0.01  (-0.06, 0.07) | 0.00  (-0.09, 0.13) | 0.02  (-0.04, 0.09) | 0.01  (-0.04, 0.03) | 0.09  (-0.02, 0.16) |
| t0 | 1 | 0.56  (0.37, 0.73) | 0.51  (0.42, 0.73) | 0.61  (0.34, 0.74) | 0.82  (0.73, 0.89) | 0.84  (0.81, 0.87) | 0.82  (0.66, 0.95) |
| t1 | 5 | 0.60  (0.31, 0.80) | 0.63  (0.35, 0.76) | 0.56  (0.31, 0.79) | 0.82  (0.62, 0.87) | 0.84  (0.80, 0.86) | 0.81  (0.47, 0.89) |
| t1+ | 4 | - | - | 0.77  (0.66, 0.79) | - | - | 0.91  (0.86, 0.91) |
| PTSD; *n* (%) |  |  |  |  |  |  |  |
| t0 | 0 | 15 (71.4%) | 9 (90.0%) | 6 (54.5%) | 10 (76.9%) | 5 (83.3%) | 5 (71.4%) |
| t1 | 5 | 10 (55.6%) | 1 (14.3%) | 9 (81.8%) | 3 (27.3%) | 0 (0.0%) | 3 (42.9%) |
| Remission from t0 to t1\* | 4 | 5 (41.7%) | 5 (83.3%) | 0 (0.0%) | 7 (77.8%) | 4 (100.0%) | 3 (60.0%) |

Overall, there are 25 dyads - 12 dyads in the iCBT group and 13 dyads in the WL control group. Note that each dyad comprises one patient and one spouse. Outcomes are summarized as median with first and third quartile (Q1, Q3) or as absolute (*n*) and relative frequency (%). Percentages refer to number of participants with information for the respective value; number of participants with missing values are provided. Values are provided for several time points: t0, start of intervention (iCBT group) / waiting (WL control group); t1, end of intervention (iCBT group) / waiting (WL control group); t1+, end of intervention in WL control group. Abbreviations: -, not applicable; #, number of; ; BSI-18, Brief Symptom Inventory-18; CAPS-5, Clinician-Administered PTSD Scale for DSM-5; EQ-5D-5L, Health questionnaire of the EuroQol group in five dimensions with five levels; iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; PCL-5, PTSD Checklist for DSM-5; PTSD, post-traumatic stress disorder; RAS, Relationship Satisfaction Scale; WL, waitlist.

\* Both percentage and number of missing values refer to number of participants with PTSD at t0.

a Total scores of the PCL-5 range from 0 to 80 (higher scores indicate greater severity of PTSD symptoms). PCL-5 was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

b Total scores of BSI-18 range from 0 to 72 (higher scores indicate greater severity of symptoms). BSI-18 was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

c RAS mean scores range from 1 to 7 (higher scores represent higher relationship satisfaction). RAS was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

d Total scores of EQ-5D-5L range from -0,661 to 1 (lower scores indicating worse quality of life), anchored at 0 (death) and 1 (perfect health). EQ-5D-5L was self-reported by participants at first login to the REPAIR web portal before starting treatment / waiting period.

**Table S4.** Results for PCL-5 (PTSD Checklist for DSM-5) change from generalized estimating equation (GEE) modelling.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | ITT (best-case/worst-case) | | ITT (MICE) | | PP | |
| Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value |
| *Multivariable models I* | | | | | | |
| iCBT [ref.: no] | -0.96 (-5.88, 3.97) | 0.703 | 4.01 (-1.89, 9.91) | 0.181 | 2.40 (-2.29, 7.08) | 0.316 |
| Baseline value (t0) | 0.09 (-0.05, 0.23) | 0.225 | 0.16 (-0.02, 0.33) | 0.078 | 0.10 (-0.03, 0.23) | 0.123 |
| *Multivariable models II* | | | | | | |
| iCBT [ref.: no] | -1.80 (-5.90, 2.30) | 0.39 | 3.74 (-2.15, 9.64) | 0.212 | 1.53 (-2.79, 5.84) | 0.488 |
| Both suffering from PTSD [ref.: no] | 0.06 (-0.09, 0.20) | 0.445 | 0.14 (-0.03, 0.30) | 0.098 | 0.09 (-0.03, 0.21) | 0.154 |
| Baseline value (t0) | -1.80 (-5.90, 2.30) | 0.390 | 3.74 (-2.15, 9.64) | 0.212 | 1.53 (-2.79, 5.84) | 0.488 |
| *Multivariable models III* | | | | | | |
| iCBT [ref.: no] | -0.21 (-3.99, 3.57) | 0.913 | 5.90 (0.05, 11.75) | 0.048 | 4.11 (0.66, 7.55) | 0.019 |
| Both suffering from PTSD [ref.: no] | 0.04 (-0.15, 0.22) | 0.700 | 0.06 (-0.15, 0.26) | 0.579 | 0.04 (-0.09, 0.17) | 0.555 |
| Baseline value (t0) | -0.21 (-0.48, 0.06) | 0.134 | -0.36 (-0.71, -0.02) | 0.04 | -0.31 (-0.60, -0.02) | 0.034 |
| Age, in years | 0.80 (-4.84, 6.45) | 0.780 | 3.03 (-2.67, 8.72) | 0.297 | 2.34 (-3.15, 7.82) | 0.404 |
| Post-ICU patient [ref.: no] | -3.94 (-7.75, -0.13) | 0.043 | -1.32 (-6.44, 3.79) | 0.611 | -3.37 (-7.29, 0.55) | 0.092 |
| Pre-existing mental disorder [ref.: no] | -0.21 (-3.99, 3.57) | 0.913 | 5.90 (0.05, 11.75) | 0.048 | 4.11 (0.66, 7.55) | 0.019 |

Model coefficients (mean difference) together with 95% confidence intervals (CIs) and *p*-values are provided. Results from both intention-to-treat (ITT) approaches (best-case/worst-case as main analysis, multiple imputation by chained equations (MICE) as sensitivity analysis) and the per-protocol (PP) analyses (sensitivity analysis) are provided. For binary variables, the reference category (ref.) is provided. Note that there were five participants in the iCBT group and none in the waitlist control group with missing information (missing PCL-5 change: 5, missing baseline value: 1; Supplemental Digital Content 1, Additional Figures A3 and A4). Abbreviations: iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; PTSD, post-traumatic stress disorder; t0, time point at beginning of intervention/waiting.

**Table S5.** Results for RAS (Relationship Satisfaction Scale) change from generalized estimating equation (GEE) modelling.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | ITT (best-case/worst-case) | | ITT (MICE) | | PP | |
| Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value |
| *Multivariable models I* | | | | | | |
| iCBT [ref.: no] | 1.11 (0.64, 1.57) | <0.001 | 0.72 (0.19, 1.26) | 0.008 | 0.80 (0.23, 1.37) | 0.006 |
| Baseline value (t0) | 0.12 (-0.07, 0.32) | 0.214 | -0.01 (-0.27, 0.25) | 0.933 | 0.07 (-0.20, 0.34) | 0.604 |
| *Multivariable models II* | | | | | | |
| iCBT [ref.: no] | 1.43 (0.76, 2.10) | <0.001 | 0.72 (0.19, 1.25) | 0.008 | 0.91 (0.45, 1.38) | <0.001 |
| Both suffering from PTSD [ref.: no] | 0.03 (-0.19, 0.25) | 0.774 | 0.00 (-0.25, 0.26) | 0.991 | 0.15 (-0.05, 0.36) | 0.142 |
| Baseline value (t0) | 1.43 (0.76, 2.10) | <0.001 | 0.72 (0.19, 1.25) | 0.008 | 0.91 (0.45, 1.38) | <0.001 |
| *Multivariable models III* | | | | | | |
| iCBT [ref.: no] | 1.23 (0.92, 1.53) | <0.001 | 0.87 (0.36, 1.39) | 0.001 | 1.05 (0.66, 1.44) | <0.001 |
| Both suffering from PTSD [ref.: no] | 0.11 (-0.01, 0.24) | 0.079 | 0.05 (-0.16, 0.26) | 0.643 | 0.10 (-0.07, 0.28) | 0.255 |
| Baseline value (t0) | -0.01 (-0.03, 0.01) | 0.332 | -0.01 (-0.04, 0.02) | 0.494 | -0.01 (-0.03, 0.02) | 0.619 |
| Age, in years | 0.67 (0.14, 1.20) | 0.013 | 0.49 (-0.04, 1.02) | 0.069 | 0.68 (0.12, 1.24) | 0.018 |
| Post-ICU patient [ref.: no] | -0.07 (-0.30, 0.15) | 0.528 | -0.22 (-0.69, 0.26) | 0.369 | -0.15 (-0.48, 0.17) | 0.353 |
| Pre-existing mental disorder [ref.: no] | 1.23 (0.92, 1.53) | <0.001 | 0.87 (0.36, 1.39) | 0.001 | 1.05 (0.66, 1.44) | <0.001 |

Model coefficients (mean difference) together with 95% confidence intervals (CIs) and *p*-values are provided. Results from both intention-to-treat (ITT) approaches (best-case/worst-case as main analysis, multiple imputation by chained equations (MICE) as sensitivity analysis) and the per-protocol (PP) analyses (sensitivity analysis) are provided. For binary variables, the reference category (ref.) is provided. Note that there were five participants in the iCBT group and none in the waitlist control group with missing information (missing RAS change: 5, missing baseline value: 1; Supplemental Digital Content 1, Additional Figures A3 and A4). Abbreviations: iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; PTSD, post-traumatic stress disorder; t0, time point at beginning of intervention/waiting.

**Table S6.** Results for remission from generalized estimating equation (GEE) modelling.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | ITT (best-case/worst-case) | | | ITT (MICE) | | PP | |
| OR (95% CI) | *p*-value | OR (95% CI) | | *p*-value | OR (95% CI) | *p*-value |
| *Multivariable models I* | | | | | | | |
| iCBT [ref.: no] | 4.28 (0.89, 20.65) | 0.070 | 4.28 (0.89, 20.65) | | 0.070 | 21.97 (2.22, 217.80) | 0.008 |
| *Multivariable models II* | | | | | | | |
| iCBT [ref.: no] | 4.05 (0.80, 20.45) | 0.090 | 4.05 (0.80, 20.45) | | 0.090 | 35.33 (3.40, 367.00) | 0.003 |
| Both suffering from PTSD [ref.: no] | 0.74 (0.14, 3.98) | 0.728 | 0.74 (0.14, 3.98) | | 0.728 | 3.37 (0.32, 35.68) | 0.314 |

Note that results are based on those dyad members with PTSD diagnosis according to CAPS-5 at t0 (iCBT: 14 participants, WL: 11 participants; Supplemental Digital Content 2, Supplemental Table S2). Furthermore, all former ICU patients with remission were treated and in each dyad comprising a spouse without remission was a former ICU patient with PTSD. Odds ratios (OR) together with 95% confidence intervals (CIs) and *p*-values are provided. Results from both intention-to-treat (ITT) approaches (best-case/worst-case as main analysis, multiple imputation by chained equations (MICE) as sensitivity analysis) and the per-protocol (PP) analyses (sensitivity analysis) are provided. For binary variables, the reference category (ref.) is provided. Note that there were four participants in the iCBT group and none in the waitlist control group with missing information on remission (Supplemental Digital Content 2, Supplemental Table A3 and A4). Furthermore, the multivariable models III were not applied – due to the small sample size. Abbreviations: iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; PTSD, post-traumatic stress disorder; t0, time point at beginning of intervention/waiting.

**Table S7.** Results for BSI-18 (Brief Symptom Inventory-18) change from generalized estimating equation (GEE) modelling.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | ITT (best-case/worst-case) | | ITT (MICE) | | PP | |
| Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value |
| *Multivariable models I* | | | | | | |
| iCBT [ref.: no] | 0.26 (-4.70, 5.21) | 0.919 | 4.36 (-1.58, 10.30) | 0.149 | 3.24 (-1.49, 7.97) | 0.180 |
| Baseline value (t0) | -0.09 (-0.25, 0.07) | 0.279 | 0.00 (-0.20, 0.20) | 0.978 | -0.05 (-0.19, 0.10) | 0.534 |
| *Multivariable models II* | | | | | | |
| iCBT [ref.: no] | -0.29 (-4.71, 4.14) | 0.899 | 4.21 (-1.74, 10.16) | 0.164 | 2.59 (-1.45, 6.64) | 0.209 |
| Both suffering from PTSD [ref.: no] | -0.12 (-0.26, 0.02) | 0.088 | -0.02 (-0.23, 0.18) | 0.823 | -0.07 (-0.21, 0.07) | 0.329 |
| Baseline value (t0) | -0.29 (-4.71, 4.14) | 0.899 | 4.21 (-1.74, 10.16) | 0.164 | 2.59 (-1.45, 6.64) | 0.209 |
| *Multivariable models III* | | | | | | |
| iCBT [ref.: no] | 0.01 (-4.08, 4.10) | 0.996 | 5.20 (-0.87, 11.27) | 0.092 | 2.84 (-1.28, 6.96) | 0.176 |
| Both suffering from PTSD [ref.: no] | -0.10 (-0.26, 0.06) | 0.234 | -0.02 (-0.25, 0.21) | 0.846 | -0.07 (-0.23, 0.10) | 0.435 |
| Baseline value (t0) | 0.05 (-0.22, 0.32) | 0.738 | -0.08 (-0.44, 0.29) | 0.678 | 0.05 (-0.32, 0.41) | 0.800 |
| Age, in years | 2.03 (-3.88, 7.94) | 0.500 | 2.91 (-4.16, 9.97) | 0.419 | 4.00 (-2.41, 10.40) | 0.221 |
| Post-ICU patient [ref.: no] | -3.94 (-8.54, 0.67) | 0.094 | -2.91 (-8.91, 3.10) | 0.342 | -3.28 (-8.77, 2.20) | 0.241 |
| Pre-existing mental disorder [ref.: no] | 0.01 (-4.08, 4.10) | 0.996 | 5.20 (-0.87, 11.27) | 0.092 | 2.84 (-1.28, 6.96) | 0.176 |

Model coefficients (mean difference) together with 95% confidence intervals (CIs) and *p*-values are provided. Results from both intention-to-treat (ITT) approaches (best-case/worst-case as main analysis, multiple imputation by chained equations (MICE) as sensitivity analysis) and the per-protocol (PP) analyses (sensitivity analysis) are provided. For binary variables, the reference category (ref.) is provided. Note that there were five participants in the iCBT group and none in the waitlist control group with missing information (missing BSI-18 change: 5, missing baseline value: 1; Supplemental Digital Content 1, Additional Figures A3 and A4). Abbreviations: iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; PTSD, post-traumatic stress disorder; t0, time point at beginning of intervention/waiting.

**Table S8.** Results for EQ-5D-5L (Health questionnaire of the EuroQol group in five dimensions with five levels) change in utility values from generalized estimating equation (GEE) modelling.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | ITT (best-case/worst-case) | | ITT (MICE) | | PP | |
| Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value | Mean difference (95% CI) | *p*-value |
| *Multivariable models I* | | | | | | |
| iCBT [ref.: no] | 0.04 (-0.07, 0.15) | 0.499 | -0.02 (-0.17, 0.13) | 0.805 | -0.01 (-0.12, 0.09) | 0.777 |
| Baseline value (t0) | 0.19 (-0.07, 0.46) | 0.150 | 0.27 (-0.02, 0.57) | 0.065 | 0.24 (-0.07, 0.55) | 0.133 |
| *Multivariable models II* | | | | | | |
| iCBT [ref.: no] | 0.04 (-0.07, 0.15) | 0.494 | -0.02 (-0.18, 0.14) | 0.800 | -0.03 (-0.14, 0.09) | 0.666 |
| Both suffering from PTSD [ref.: no] | 0.01 (-0.11, 0.14) | 0.844 | -0.02 (-0.16, 0.12) | 0.775 | -0.04 (-0.18, 0.09) | 0.537 |
| Baseline value (t0) | 0.19 (-0.08, 0.45) | 0.168 | 0.28 (0.00, 0.57) | 0.050 | 0.27 (-0.04, 0.57) | 0.091 |
| *Multivariable models III* | | | | | | |
| iCBT [ref.: no] | -0.01 (-0.11, 0.09) | 0.865 | -0.07 (-0.23, 0.09) | 0.389 | -0.07 (-0.18, 0.03) | 0.172 |
| Suffering from PTSD [ref.: no] | 0.01 (-0.10, 0.11) | 0.925 | -0.02 (-0.15, 0.11) | 0.772 | -0.05 (-0.16, 0.06) | 0.416 |
| Baseline value (t0) | 0.30 (-0.05, 0.64) | 0.089 | 0.36 (-0.01, 0.73) | 0.058 | 0.33 (-0.06, 0.71) | 0.095 |
| Age, in years | 0.00 (0.00, 0.01) | 0.424 | 0.00 (0.00, 0.01) | 0.318 | 0.00 (0.00, 0.01) | 0.375 |
| Post-ICU patient [ref.: no] | 0.05 (-0.12, 0.22) | 0.553 | 0.04 (-0.15, 0.24) | 0.671 | 0.02 (-0.16, 0.20) | 0.811 |
| Pre-existing mental disorder [ref.: no] | 0.13 (0.02, 0.24) | 0.018 | 0.10 (-0.03, 0.23) | 0.124 | 0.11 (-0.01, 0.22) | 0.064 |

Model coefficients (mean difference) together with 95% confidence intervals (CIs) and *p*-values are provided. Results from both intention-to-treat (ITT) approaches (best-case/worst-case as main analysis, multiple imputation by chained equations (MICE) as sensitivity analysis) and the per-protocol (PP) analyses (sensitivity analysis) are provided. For binary variables, the reference category (ref.) is provided. Note that there were five participants in the iCBT group and none in the waitlist control group with missing information (missing EQ-5D-5L change: 5, missing baseline value: 1; Supplemental Digital Content 1, Additional Figures A3 and A4). Abbreviations: iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; PTSD, post-traumatic stress disorder; t0, time point at beginning of intervention/waiting.

**Table S9.** Between-group effect sizes (Cohen´s d, standardized mean differences) for pre-post changes in primary and secondary outcomes

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | ITT (best-case/worst-case) | ITT (MICE) | PP |
| Effect size *d* (95% CI) | Effect size *d* (95% CI) | Effect size *d* (95% CI) |
| *Primary outcome* | | | |
| PCL-5 | -0.14 (-0.81, 0.54) | 0.48 (-0.21, 1.16) | 0.40 (-0.35, 1.16) |
| *Secondary outcomes* | | | |
| RAS | 1.67 (0.89, 2.45) | 0.94 (0.23, 1.65) | 1.10 (0.30, 1.90) |
| BSI-18 | 0.04 (-0.64, 0.71) | 0.51 (-0.17, 1.20) | 0.54 (-0.22, 1.30) |
| EQ-5D-5L | 0.25 (-0.42, 0.93) | 0.09 (-0.58, 0.77) | 0.07 (-0.68, 0.83) |

Effect sizes with 95% confidence intervals (CI) were derived from the main analyses with generalized estimating equation (GEE) modelling (Multivariable models I; Table 2, Supplemental Tables S5, S7, S8 in Supplemental Digital Content 2). Abbreviations: BSI-18, Brief Symptom Inventory-18; EQ-5D-5L, Health questionnaire of the EuroQol group in five dimensions with five levels; ITT, intention-to-treat; PCL-5, PTSD Checklist for DSM-5; RAS, Relationship Satisfaction Scale.

**Table S10.** Overview about safety variables - overall as well as stratified by treatment group.

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Overall | Treatment group | |
| iCBT | WL control |
| Number of suicide alerts |  |  |  |
| False alarm; n | 3 | 3 | 0 |
| Caused by reasons not related to the study; n | 2 | 0 | 2 |
| Clinical relevant PCL-5 deterioration; *n* (%)\* | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Premature termination |  |  |  |
| Between randomization and t0; *n* (%) | 1 (2.0%) | 1 (4.2%) | 0 (0.0%) |
| Between t0 and t1; *n* (%) | 8 (16.0%) | 6 (25.0%) | 2 (7.7%) |
| Between t1 and t1+; *n* (%) | - | - | 10 (38.5%) |

Overall, there are 25 dyads - 12 dyads in the iCBT group and 13 dyads in the WL control group. Note that each dyad comprises one patient and one spouse. A PCL-5 (PTSD Checklist for DSM-5) change of 10 or more points is regarded as clinically relevant. Outcomes are summarized as absolute (*n*) and relative frequencies (%). Percentages refer to number of participants with information for the respective value. Values are provided for several time points: t0, start of intervention (iCBT group) / waiting (WL control group); t1, end of intervention (iCBT group) / waiting (WL control group); t1+, end of intervention in WL control group. Abbreviations: -, not applicable; iCBT, internet-based cognitive-behavioral writing therapy; WL, waitlist.

\* missing for 9 participants (iCBT: 7 participants (post-ICU patient: 4, spouse: 3), WL control: 2 participants (spouse: 2))

**Table S11.** Overview about safety variables - overall as well as stratified by post-ICU patient/spouse status and by treatment group.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | Post-ICU patient | | | Spouse | | |
| overall | Treatment group | | overall | Treatment group | |
| iCBT | WL control | iCBT | WL control |
| Number of suicide alerts |  |  |  |  |  |  |
| False alarm; n | 2 | 2 | 0 | 1 | 1 | 0 |
| Caused by reasons not related to the study; n | 2 | 0 | 2 | 0 | 0 | 0 |
| Clinical relevant PCL-5 deterioration; *n* (%)\* | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Premature termination |  |  |  |  |  |  |
| Between randomisation and t0; *n* (%) | 1 (4.0%) | 1 (8.3%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Between t0 and t1; *n* (%) | 3 (12.0%) | 3 (25.0%) | 0 (0.0%) | 5 (20.0%) | 3 (25.0%) | 2 (15.4%) |
| Between t1 and t1+; *n* (%) | - | - | 4 (30.8%) | - | - | 6 (46.2%) |

Overall, there are 25 dyads - 12 dyads in the iCBT group and 13 dyads in the WL control group. Note that each dyad comprises one patient and one spouse. A PCL-5 (PTSD Checklist for DSM-5) change of 10 or more points is regarded as clinically relevant. Outcomes are summarized as absolute (*n*) and relative frequencies (%). Percentages refer to number of participants with information for the respective value. Values are provided for several time points: t0, start of intervention (iCBT group) / waiting (WL control group); t1, end of intervention (iCBT group) / waiting (WL control group); t1+, end of intervention in WL control group. Abbreviations: -, not applicable; iCBT, internet-based cognitive-behavioral writing therapy; ICU, intensive care unit; WL, waitlist.

\* missing for 9 patients (intervention: 7 participants (former ICU patient: 4, spouse: 3), waitlist: 2 participants (spouse: 2))

**Table S12.** Dyadic concordance in treatment effects in terms of PCL-5 (PTSD Checklist for DSM-5) change.

|  |  |  |  |
| --- | --- | --- | --- |
| Dyad member suffering from PTSD | ITT  (best-case/worst-case) | ITT  (MICE) | PP |
| Only one | 0.29 (-0.24, 0.68) | 0.43 (-0.06, 0.92) | 0.32 (-0.31, 0.76) |
| Both | -0.25 (-0.79, 0.49) | -0.06 (-0.95, 0.84) | -0.58 (-0.95, 0.44) |

Spearman correlation together with 95% confidence intervals are provided. Analysis was stratified by the number of dyad members suffering from post-traumatic stress disorder (PTSD). Results from both intention-to-treat (ITT) approaches (best-case/worst-case substitution as main analysis, multiple imputation by chained equations (MICE) as sensitivity analysis) and the per-protocol (PP) analyses are provided. Note that there were nine participants with missing information on PCL-5 change (Supplemental Digital Content 1, Additional Figures A1 and A2).