

Multimedia Appendix 3

Supplementary results to

[The effect of an internet-based cognitive behavioural therapy programme adapted to patients with cardiovascular disease and depression – a randomised controlled study]

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Results based on mixed model analysis using multiple imputed data.

The final mixed model analysis on multiple imputed data showed a significant effect of iCBT compared to ODF on PHQ-9 ($P=.002$), MADRS-S ($P <.001.$), EQ-VAS ($P <.001.$) and MCS ($P <.001.$) There was no significant difference between iCBT and ODF with regard to PCS ($P=.26$). Effect sizes calculated on multiple imputed data indicate moderate effects of iCBT on depression and HRQoL, (Table A1).

Table A1: Treatment effects

All data is imputed using multiple imputation. Data are mean (SD) unless otherwise stated. SD is pooled in

accordance with the following equation: $S_{pooled} = \sqrt{\frac{(n_1-1)s_1^2 + (n_2-1)s_2^2 + \dots + (n_k-1)s_k^2}{n_1+n_2+\dots+n_k-k}}$

| | iCBT (n=72) | | ODF (n=72) | | Estimate for iCBT and time interaction, 95% CI | | P | Effect size (d) |
|---------|---------------|---------------|---------------|---------------|--|----------------|--------|-----------------|
| | Baseline | 9 weeks | Baseline | 9 weeks | | | | |
| PHQ-9 | 10.71 (4.47) | 6.39 (4.71) | 10.22 (5.19) | 8.30 (4.65) | -2.40 | -3.93 to -0.87 | .002 | 0.51 |
| MADRS-S | 18.01 (7.25) | 10.57 (7.51) | 17.67 (6.31) | 15.60 (8.26) | -5.38 | -7.84 to -2.92 | <.001. | 0.71 |
| EQ-VAS | 53.56 (20.09) | 65.34 (21.84) | 57.36 (18.47) | 56.27 (22.72) | 12.86 | 6.29 to 19.44 | <.001. | 0.64 |
| PCS12 | 39.80 (10.09) | 42.05 (10.63) | 37.79 (11.22) | 38.32 (11.71) | 1.72 | -1.28 to 4.72 | .26 | 0.19 |
| MCS12 | 36.08 (9.36) | 43.62 (11.37) | 36.41 (10.00) | 38.18 (11.00) | 5.77 | 2.39 to 9.16 | <.001. | 0.56 |

PHQ-9= Patient Health Questionnaire 9. MADRS-S= Montgomery Åsberg Depression Rating Scale (self-rating version). EQ-VAS = EuroQoL Visual Analogue Scale. PCS12= Physical Component Score of the Short Form 12. MCS12= Mental Component Score of the Short Form 12.

Per protocol analyses

The per-protocol analysis was divided into two parts. In the first analysis all participants in the iCBT group that had completed at least one module in iCBT (n=64) was compared to those who had performed at least one activity in the ODF (n=46) (Table A2). This analysis showed a significant effect of iCBT on depression (PHQ-9 mean between group difference - 2.72 ($P<.001.$) with a moderate effect size ($d=0.69$). Depression as measured by MADRS-S showed a significant ($P<.001.$) and large effect size (0.87). HRQoL as measured by EQ-VAS

and MCS showed a significant difference favouring iCBT ($P<.001.$) and, $P<.001.$) For the PCS no significant difference was found ($p=.39$).

Table A2: Treatment effect per-protocol

Observed data on participants with at least one iCBT module or ODF activity. Data are mean (SD) unless otherwise stated.

| | iCBT (n=64) | | ODF (n=46) | | Mean between-group treatment difference (95% CI) | | P | Effect size (d) |
|---------|---------------|---------------|---------------|---------------|--|----------------|--------|-----------------|
| | Baseline | 9 weeks | Baseline | 9 weeks | | | | |
| PHQ-9 | 10.74 (4.56) | 6.30 (4.79) | 10.14 (5.11) | 8.63 (4.53) | -2.72 | -4.24 to -1.20 | <.001. | 0.69 |
| MADRS-S | 18.19 (6.96) | 10.30 (7.42) | 17.86 (5.76) | 16.21 (8.34) | -5.95 | -8.56 to -3.34 | <.001. | 0.87 |
| EQ-VAS | 53.12 (20.22) | 66.14 (21.69) | 58.73 (17.87) | 58.46 (21.92) | 11.56 | 4.88 to 18.25 | <.001. | 0.66 |
| PCS12 | 39.79 (10.16) | 42.38 (10.74) | 39.98 (10.32) | 41.26 (11.06) | 1.31 | -1.76 to 4.38 | .39 | 0.16 |
| MCS12 | 35.80 (9.33) | 43.94 (11.41) | 36.45 (10.49) | 36.81 (10.75) | 7.17 | 3.70 to 10.63 | <.001. | 0.79 |

PHQ-9= Patient Health Questionnaire 9. MADRS-S= Montgomery Åsberg Depression Rating Scale (self-rating version). EQ-VAS = EuroQoL Visual Analogue Scale. PCS= Physical Component Score of the Short Form 12. MCS= Mental Component Score of the Short Form 12.

In the second per-protocol analysis those participants in the iCBT group that had completed the full programme (i.e. seven modules, n=43) were compared to those in the ODF (n=20) who had performed at least nine activities (n=20) (Table A3). This analysis revealed a significant effect of iCBT on depression (PHQ-9 mean between group difference -3.56 ($P=.002$) with a large effect size ($d=0.89$). Depression as measured by MADRS-S showed a significant ($P=.002$) and large effect size (.90). HRQoL as measured by EQ-VAS and MCS showed a significant difference favouring iCBT ($P<.001.$ and) $P<.001.$ As for the PCS no significant difference was found ($P=.26$).

Table A3. Treatment effect per-protocol

Observed data on participants with seven iCBT modules or at least nine ODF activities. Data are mean (SD) unless otherwise stated.

| | iCBT (n=43) | | ODF (n=20) | | Mean between-group treatment difference (95% CI) | | <i>P</i> | Effect size (d) |
|---------|---------------|---------------|---------------|---------------|--|-----------------|----------|-----------------|
| | Baseline | 9 weeks | Baseline | 9 weeks | | | | |
| PHQ-9 | 10.86 (4.87) | 6.09 (5.11) | 11.15 (6.07) | 9.80 (4.00) | -3.56 | -5.74 to -1.37 | .002 | 0.89 |
| MADRS-S | 18.12 (7.16) | 9.88 (7.95) | 20.00 (6.77) | 17.35 (8.67) | -6.29 | -10.08 to -2.50 | .002 | 0.90 |
| EQ-VAS | 50.35 (20.19) | 66.12 (22.80) | 55.90 (16.89) | 52.15 (22.27) | 18.19 | 8.67 to 27.71 | <.001. | 1.03 |
| PCS12 | 38.21 (8.79) | 41.96 (11.04) | 39.93 (11.07) | 40.73 (12.44) | 2.62 | -2.01 to 7.25 | .26 | 0.31 |
| MCS12 | 35.90 (9.83) | 44.93 (12.28) | 34.34 (10.06) | 34.10 (8.54) | 9.80 | 4.78 to 14.83 | <.001. | 1.06 |

PHQ-9= Patient Health Questionnaire 9. MADRS-S= Montgomery Åsberg Depression Rating Scale (self-rating version). EQ-VAS = EuroQol Visual Analogue Scale. PCS12= Physical Component Score of the Short Form 12. MCS12= Mental Component Score of the Short Form 12.