Two Decades of Digital Interventions for Anxiety Disorders: A Systematic Review and Meta-Analysis of Treatment Effectiveness

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Other Supplementary Material

**eAppendix 1.** Search strings from PubMed

Psychotherapy[MH] OR psychotherap\*[All Fields] OR cbt[All Fields] OR "behavior therapies"[All Fields] OR "behavior therapy"[All Fields] OR "behavior therapeutic"[All Fields] OR "behavior therapeutical"[All Fields] OR "behavior therapeutics"[All Fields] OR "behavior therapeutist"[all Fields] OR "behavior therapeutists"[All Fields] OR "behavior treatment"[All Fields] OR "behavior treatments"[All Fields] OR "behaviors therapies"[All Fields] OR "behaviors therapy"[All Fields] OR "behaviors therapeutics"[All Fields] OR "behaviors therapeutic"[All Fields] OR "behaviors therapeutical"[All Fields] OR "behaviors therapeutist"[All Fields] OR "behaviors therapeutists"[All Fields] OR "behaviors treatment"[All Fields] OR "behaviors treatments"[All Fields] OR "behavioral therapies"[All Fields] OR "behavioral therapy"[All Fields] OR "behavioral therapeutics"[All Fields] OR "behavioral therapeutic"[All Fields] OR "behavioral therapeutical"[All Fields] OR "behavioral therapeutist"[All Fields] OR 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"behavioral activation"[All Fields] OR "cognitive therapies"[All Fields] OR "cognitive therapy"[All Fields] OR "cognitive therapeutic"[All Fields] OR "cognitive therapeutics"[All Fields] OR "cognitive therapeutical"[All Fields] OR "cognitive therapeutist"[All Fields] OR "cognitive therapeutists"[All Fields] OR "cognitive treatment"[All Fields] OR "cognitive treatments"[All Fields] OR "cognitive restructuring"[All Fields] OR (("compassion-focused"[All Fields] OR "compassion-focussed"[All Fields]) AND (therapy[SH] OR therapies[All Fields] OR therapy[All Fields] OR therape\*[All Fields] OR therapis\*[All Fields]OR Therapeutics [OR treatment\*[All Fields])) OR ((therapy[SH] OR therapies[All Fields] OR therapy [All Fields] OR therape\*[All Fields] OR therapis\*[All Fields] OR Therapeutics[MH] OR treatment\*[All Fields]) AND constructivist\*[All Fields]) OR "metacognitive therapies"[All Fields] OR "metacognitive therapy"[All Fields] OR "metacognitive therapeutic"[All Fields] OR 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AND

"social anxiety"[All Fields] OR shy[All Fields] OR ("shyness"[MeSH Terms] OR "shyness"[All Fields]) OR "test anxiety"[All Fields] OR gad[All Fields] OR "generalized anxiety"[All Fields] OR "generalised anxiety"[All Fields] OR worry[All Fields] OR ("panic"[MeSH Terms] OR "panic"[All Fields]) OR (agoraphobi[All Fields] OR agoraphobia[All Fields] OR agoraphobia'[All Fields] OR agoraphobia's[All Fields] OR agoraphobias[All Fields] OR agoraphobic[All Fields] OR agoraphobic's[All Fields] OR agoraphobics[All Fields] OR agoraphobics'[All Fields] OR agoraphobie[All Fields] OR agoraphobien[All Fields]) OR "anxiety disorder"[All Fields] OR "social phobia"[All Fields] OR "social anxiety disorder"[All Fields] OR Arachnophobia[All Fields] OR Ophidiophobia[All Fields] OR Acrophobia[All Fields] OR Agoraphobia[All Fields] OR Cynophobia[All Fields] OR Claustrophobia[All Fields] OR Mysophobia[All Fields] OR Aerophobia[All Fields] OR Trypophobia[All Fields] OR Carcinophobia[All Fields] OR Thanatophobia[All Fields] OR Glossophobia[All Fields] OR Monophobia[All Fields] OR Ornithophobia[All Fields] OR Alektorophobia[All Fields] OR Trypanophobia[All Fields] OR Anthropophobia[All Fields] OR Aquaphobia[All Fields] OR Autophobia[All Fields] OR Hemophobia[All Fields] OR Xenophobia[All Fields] OR Ailurophobia[All Fields] OR Nyctophobia[All Fields] OR Phobophobia[All Fields] OR Philophobia[All Fields] OR Triskaidekaphobia[All Fields] OR Emetophobia[All Fields] OR Entomophobia[All Fields] OR Zoophobia[All Fields] OR Scelerophobia[All Fields] OR Cibophobia[All Fields] OR Tokophobia[All Fields] OR Pseudodysphagia[All Fields] OR Gerascophobia[All Fields] OR Technophobia[All Fields] OR Ergophobia[All Fields] OR Coulrophobia [All Fields] OR Photophobia[All Fields] OR Numerophobia[All Fields] OR Taphophobia

**eAppendix 2.** Pre-determined hierarchy of outcome instrument selection, per anxiety disorder

The following hierarchy was established to decide outcome measures of interest by study and primary diagnosis (Brown, 1997; Chambless, Caputo, Bright, & Gallagher, 1984; Dear et al., 2011; Khawaja, 2003; Mennin et al., 2002; Osman, Kopper, Barrios, Osman, & Wade, 1997; Rutter & Brown, 2017; Rytwinski et al., 2009; Shear et al., 2001): in GAD or mixed anxiety samples, outcome selection was prioritized by 1) Penn State Worry Questionnaire (PSWQ), 2) Generalized Anxiety Disorder-7 (GAD-7) and 3) Beck Anxiety Inventory (BAI); in PD/A samples, outcome selection was prioritized by 1) Panic Disorder Severity Scale, clinician or self-rated (PDSS, PDSS-SR), 2) Body Sensations Questionnaire (BSQ) and 3) Beck Anxiety Inventory (BAI); in SAD samples, outcome selection was prioritized by 1) Liebowitz Social Anxiety Scale, clinician or self-rated (LSAS, LSAS-SR), 2) Social Interaction Anxiety Scale (SIAS) and 3) Beck Anxiety Inventory (BAI); in Specific Phobia samples, the primary outcome measure as defined by the study was used. If none of the outcomes in the pre-determined hierarchy were used in a given study, the primary outcome measure as defined by the study was used.

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Chambless, D. L., Caputo, G. C., Bright, P., & Gallagher, R. (1984). Assessment of fear of fear in agoraphobics: the body sensations questionnaire and the agoraphobic cognitions questionnaire. Journal of consulting and clinical psychology, 52(6), 1090-1097.

Dear, B. F., Titov, N., Sunderland, M., McMillan, D., Anderson, T., Lorian, C., & Robinson, E. (2011). Psychometric comparison of the generalized anxiety disorder scale-7 and the Penn State Worry Questionnaire for measuring response during treatment of generalised anxiety disorder. Cognitive Behaviour Therapy, 40(3), 216-227. doi:10.1080/16506073.2011.582138

Khawaja, N. G. (2003). Revisiting the Factor Structure of the Agoraphobic Cognitions Questionnaire and Body Sensations Questionnaire: A Confirmatory Factor Analysis Study. Journal of Psychopathology and Behavioral Assessment, 25(1), 57-63. doi:10.1023/A:1022204104267

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**eAppendix 3.** Citations of studies included in the meta-analysis of digital interventions versus wait-list and care-as-usual control groups and supplemental analysis of digital interventions versus face-to-face treatment groups.

(Allen et al., 2016; Andersson, Carlbring, & Furmark, 2012; Andersson et al., 2006; Andersson, Paxling, et al., 2012; Andrews, 2011; Bell, Colhoun, Carter, & Frampton, 2012; Berger, Boettcher, & Caspar, 2014; Berger, Hohl, & Caspar, 2009; Berger et al., 2017; Bergstrom et al., 2010; Boettcher et al., 2014; Botella et al., 2010; P. Carlbring et al., 2006; P. Carlbring et al., 2007; P. Carlbring et al., 2011; P. Carlbring et al., 2005; Per Carlbring, Westling, Ljungstrand, Ekselius, & Andersson, 2001; Christensen et al., 2014; Ciuca, Berger, Crişan, & Miclea, 2018; Dahlin et al., 2016; Dear et al., 2015; Furmark et al., 2009; Hedman et al., 2011; Ivanova et al., 2016; Johansson et al., 2017; Johnston, Titov, Andrews, Spence, & Dear, 2011; Jones, Hadjistavropoulos, & Soucy, 2016; Kählke et al., 2019; Kenardy et al., 2003; Kiropoulos et al., 2008; Klein, Richards, & Austin, 2006; Kok, van Straten, Beekman, & Cuijpers, 2014; Mathiasen, Riper, Ehlers, Valentin, & Rosenberg, 2016; Newman, Kenardy, Herman, & Taylor, 1997; Newman, Przeworski, Consoli, & Taylor, 2014; Nordgren et al., 2014; Oromendia, Orrego, Bonillo, & Molinuevo, 2016; Paxling et al., 2011; D. Richards et al., 2016; J. C. K. Richards, B.; Austin, D. W., 2006; Robinson et al., 2010; Ruwaard, Broeksteeg, Schrieken, Emmelkamp, & Lange, 2010; Schroder, Jelinek, & Moritz, 2017; Schulz et al., 2016; Silfvernagel et al., 2012; Stolz et al., 2018; N. Titov, Andrews, Choi, Schwencke, & Mahoney, 2008; N. Titov, Andrews, Johnston, Robinson, & Spence, 2010; N. Titov et al., 2009; Nickolai Titov, Andrews, & Schwencke, 2008; N. Titov, Andrews, Schwencke, Drobny, & Einstein, 2008; Tulbure et al., 2015; van Ballegooijen et al., 2013; Wims, Titov, Andrews, & Choi, 2010)

Allen, A. R., Newby, J. M., Mackenzie, A., Smith, J., Boulton, M., Loughnan, S. A., & Andrews, G. (2016). Internet cognitive-behavioural treatment for panic disorder: randomised controlled trial and evidence of effectiveness in primary care. BJPsych Open, 2(2), 154-162. doi:10.1192/bjpo.bp.115.001826

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Andersson, G., Paxling, B., Roch-Norlund, P., Ostman, G., Norgren, A., Almlov, J., . . . Silverberg, F. (2012). Internet-based psychodynamic versus cognitive behavioral guided self-help for generalized anxiety disorder: a randomized controlled trial. Psychother Psychosom, 81(6), 344-355. doi:10.1159/000339371

Andrews, G. D., M.; Titov, N. (2011). Effectiveness randomized controlled trial of face to face versus Internet cognitive behaviour therapy for social phobia. Aust N Z J Psychiatry, 45(4), 337-340. doi:10.3109/00048674.2010.538840

Bell, C. J., Colhoun, H. C., Carter, F. A., & Frampton, C. M. (2012). Effectiveness of computerised cognitive behaviour therapy for anxiety disorders in secondary care. Aust N Z J Psychiatry, 46(7), 630-640. doi:10.1177/0004867412437345

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Carlbring, P., Nilsson-Ihrfelt, E., Waara, J., Kollenstam, C., Buhrman, M., Kaldo, V., . . . Andersson, G. (2005). Treatment of panic disorder: live therapy vs. self-help via the Internet. Behav Res Ther, 43(10), 1321-1333. doi:10.1016/j.brat.2004.10.002

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eFigure 1. Funnel plot of standard error by Hedges’ g for publication bias examination

eTable 1. Characteristics of studies and results from supplemental analysis of digital interventions versus face-to-face treatment groups.

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| **eTable 1.** |
| Characteristics and effect sizes of studies included the supplemental meta-analysis comparing digital and face-to-face interventions |
| Study | Treatment Comparison | Primary Diagnosis | Treatment Support | Outcome Measure | N | Hedges' g | NNT | RoB | Recruit. Setting | Cont. of Study |
| Newman (2014) | cCBT-G vs. F-F CBT-G | GAD | guided | BSQ | 38 | 0.13 | 13.5 | S.C. | Comm. | Oceania |
| Bergstrom (2010) | iCBT vs. F-F CBT-G | PD / A | guided | PDSS-SR | 113 | 0.00 | - | S.C. | Clin. | Europe |
| Carlbring (2005) | iCBT vs. F-F CBT | PD / A | guided | BSQ | 49 | -0.05 | 35.7 | S.C. | Comm. | Europe |
| Kenardy (2003) | cCBT vs. F-F CBT | PD / A | guided | BSQ | 122 | 0.48 | 3.7 | S.C. | Clin. | Mix |
| Kiropoulos (2008) | iCBT vs. F-F CBT | PD / A | guided | PDSS | 86 | -0.12 | 14.7 | Low | Comm. | Oceania |
| Newman (1997) | cCBT vs. F-F CBT | PD / A | guided | FQ | 20 | 0.01 | 166.7 | S.C. | Comm. | Oceania |
| Andrews (2011) | iCBT vs. F-F CBT | SAD | guided | SIAS | 31 | -0.01 | 166.7 | S.C. | Clin. | Oceania |
| Botella (2010) | iCBT vs. F-F CBT | SAD | unguided | BFNE | 98 | 0.03 | 62.5 | S.C. | Comm. | Europe |
| Hedman (2011) | iCBT vs. F-F CBT-G | SAD | guided | LSAS | 126 | 0.40 | 4.5 | Low | Clin. | Europe |
| *Note*: iCBT: internet delivered cognitive behavioral therapy; cCBT-G: computer delivered cognitive behavioral therapy group format delivered; cCBT: computer delivered cognitive behavioral therapy; F-F CBT-G: face to face cognitive behavioral therapy group format delivered; F-F CBT: face to face cognitive behavioral therapy individual format delivered; Guided: content support provided by trained/para-professional; Unguided: no content support provided; N: total sample analyzed by intention to treat; Hedges' g: effect size between treatment and control according to Hedges' g formula; Negative Hedges' g: favoring face-to-face treatment; NNT: number needed to treat; RoB: Risk of Bias by category of low, some concern (S.C.) or high; Comm.: open, public, voluntary recruitment; Clin.: clinical referral to study from a medical professional for recruiment method; Europe: continental Europe; Oceania: continent including studies from Australia and or New Zealand; Mix: sample from multiple international regions (Scotland, Australia); BSQ: Body Sensations Questionnaire; PDSS-SR: Panic Disorder Severity Scale – Self-Rated; PDSS: Panic Disorder Severity Scale; FQ: Fear Questionnaire; LSAS: Liebowitz Social Anxiety Scale; BFNE: Brief Fear of Negative Evaluation; PD / A: panid disorder with or without agoraphobia; SAD: social anxiety disorder; GAD: generalized anxiety disorder |

eTable 2. Auxiliary sensitivity and subgroup analyses

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| **eTable 2.**    |
| Auxiliary sensitivity and subgroup analyses |
| Sensitivity and subgroup categorizations | Number of Comparisons | Number of Subjects | Hedges' g | 95% CI (g) | p-value | I² | 95% CI (I²) | NNT |
| **Sensitivity Analyses** |   |   |   |   |   |   |   |   |
| Without Berger et al., 2017 | 52 | 4,819  | 0.81 | (0.68 - 0.94) | - | 76 | 68-81 | 2.3 |
| With Berger et al., 2017 | 53 | 4,958 | 0.80 | (0.68 - 0.93) | - | 75 | 68-80 | 2.3 |
| Without Med. and Treat. History | 48 | 4,372 | 0.81 | (0.68 - 0.95) | -  | 74 | 65-80 | 2.3 |
| **Subgroup Analysis** |   |   |   |   |   |   |   |   |
| **Wait-list Control Category** |   |   |   |   | 0.131 |   |   |   |
| WL | 36 | 2,814 | 0.83 | (0.68 - 0.98) | - | 70 | 56-78 | 2.3 |
| WL-UC | 5 | 702  | 0.54 | (0.33 - 0.76) | - | 39 | 0-76 | 3.4 |
| WL-OD | 8 | 689 | 0.82 | (0.63 - 1.00) | - | 26 | 0-67 | 2.3 |
| WL-IC | 4 | 753 | 1.02 | (0.25 - 1.79) | - | 92 | 83-95 | 1.9 |
|  |
| *Note:* WL: wait- list control; WL-IC: wait-list with access to information control provision; WL-OD: wait-list with access to online discussion group; WL-UC: wait-list with indicated access to usual care;; Hedges' g: effect size between treatment and control according to Hedges' g formula; 95% CI (g): 95% confidence interval for effect size (g); p-value: significance difference between the effect sizes in the subgroups at .alpha 05; I²: heterogeneity as a proportion; 95% CI (I²): 95% confidence interval for I²; NNT: number needed to treat; Berger et al., 2017: Berger, T., Urech, A., Krieger, T., Stolz, T., Schulz, A., Vincent, A., . . . Meyer, B. (2017). Effects of a transdiagnostic unguided Internet intervention ('velibra') for anxiety disorders in primary care: results of a randomized controlled trial. Psychol Med, 47(1), 67-80. doi:10.1017/s0033291716002270; Without Med. and Treatment History: studies which did not report current or past medication use or treatment history as part of demographic information compared between treatment and control groups (Botella et al., 2010; Kenardy et al., 2013; Kok et al., 2014; Oromendia et al., 2016; van Ballegooijen et al., 2013). |