



Internet-Delivered Psychological Treatment Options for Panic Disorder: A Review on Their Efficacy and Acceptability

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Background Internet-delivered psychological treatments have been suggested as a chance to expand the access to professional help. However, little is known about the usefulness of different support formats and approaches of digital treatments for panic disorder among clinicians.

Objective This narrative review aimed to explore the recent evidence base on the efficacy and acceptability of different internet-delivered treatments for adults with panic disorder.

Methods A systematic search in electronic databases (Pubmed/Medline, PSYINDEX) and a hand search were performed to identify articles on randomized controlled trials published within the past five years (2012/12/10–2017/12/12) in English peer-reviewed journals.

Results Eight studies (1,013 participants) involving 10 interventions met the inclusion criteria. Nine interventions were primarily based on Cognitive Behavioral Therapy principles. Most interventions were effective, when compared to a control condition (6 of 8 comparisons). Minimal guidance was associated with improved outcomes in one study and adherence in two studies (3 comparisons). Furthermore, no differences were found based on treatment approach (2 comparisons). Regarding acceptability, the attrition rates were moderate to high, ranging from 9.8% to 42.1% of randomized participants. Adherence rates also varied largely (7.8–75%), whereas participant satisfaction of program completers was assessed overall high (5 studies).

Conclusion Diverse effective internet-delivered treatments are available for the self-management of panic symptoms. Especially self-guided and transdiagnostic Cognitive Behavioral Therapy approaches appear being efficient options for the dissemination in routine care. However, due to the limited evidence base, further efforts are required to improve the actual uptake of internet-delivered treatments and identify moderators of outcomes.

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Key Words Panic disorder, Anxiety disorder, eHealth, Cognitive behavior therapy, Internet.

INTRODUCTION

Anxiety disorders considerably contribute to the global burden of mental disease due to their high incidence, tendency to chronification and comorbidity.¹⁻³ Panic disorder (PD), respectively PD with agoraphobia (PDA), is the most common anxiety disorder during early adulthood,³ with an estimated lifetime prevalence of 1.7%, and 80.4% of persons with PD having a lifetime comorbid mental disorder.⁴ Since recurrent panic attacks and worries decrease subjective well-being, qual-

ity of life and psychosocial functioning,⁵ untreated PD is associated with a higher risk of disability.⁶

In addition to pharmacotherapy, different evidence-based psychological treatment options are available for PD,^{6,7} such as, Cognitive Behavioral Therapy (CBT).⁸ Yet, persistent treatment gaps⁹ hamper the access to such treatments in health care. Moreover, especially young adults with anxiety appear to prefer online self-help over face-to-face services.¹⁰ Internet-delivered psychological treatments have been proposed as an option to expand the access to therapy¹¹ as they provide additional options for the dissemination of psychological treatments for persons not able or not willing to use face-to-face services.^{12,13} Several internet treatments are available, differing in principle, support format and treatment approach. While most internet treatments are based on the principles of CBT,¹⁴ Mindfulness Cognitive Therapy,^{15,16} Acceptance Commitment Therapy (ACT)¹⁷ and psychodynamic therapy¹⁸ have also been transferred to Internet-delivery.

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In recent years, most research efforts and advances were associated with internet-delivered CBT (iCBT) programs. ICBT for PD delivers the same components like traditional face-to-face CBT, such as psychoeducation, cognitive restructuring, de-arousal and exposure, as online self-help format.¹⁹ Like CBT, iCBT can reduce the frequency of panic attacks and avoidance behavior in most patients, whereas psychoeducation alone and pure self-help are suitable options for milder, recently manifested PD forms.²⁰ As common support formats, self-guided and clinician-guided internet treatments are provided, whereas the latter typically combine structured self-help content with minimal scheduled support, for instance, via email or telephone.^{21,22} Although most treatment approaches are disorder-specific, transdiagnostic tailored internet treatments are of increasing relevance as they allow for simultaneous treatment²³ and thereby address comorbidity and overlapping symptoms in anxiety disorders.²⁴

Numerous randomized controlled trials (RCTs) have demonstrated the effectiveness of internet treatments for anxiety disorders.^{14,25-27} Furthermore, research evidence indicated an equivalent effectiveness of guided iCBT with face-to-face CBT²⁸⁻³⁰ and that iCBT for PD can be successfully provided under routine care conditions.^{31,32} Conversely, still little is known about specific features such as support format and treatment approach making iCBT effective.²¹ For instance, while some reviews identified that guidance appears to improve therapeutic effects of iCBT for anxiety disorders,^{26,33,34} Others¹⁴ indicated no substantial impact. Furthermore, findings regarding the role of treatment approaches are undecided, but suggest higher effects of more established disorder-specific treatments. Nonetheless, recent meta-analyses³⁵⁻³⁷ also identified medium to large effect sizes for transdiagnostic and tailored iCBT for anxiety disorders, when compared to a wait-list control (WLC), active control conditions or care as usual (CAU). Hence, it would be interesting to determine which treatments work best for persons with PD.

Moreover, or the successful dissemination of internet treatments for PD the acceptance of patients is an important precondition.¹⁵ Acceptability of iCBT is generally rated as high.³⁸ For instance, a systematic review¹⁴ showed high participant satisfaction in therapist-guided iCBT for anxiety disorders. These positive findings that were collected from program completers, however, could be biased, since attrition rates are often high in studies on internet treatments for anxiety disorders.²⁶ Adherence rates also vary largely. According to a systematic review on transdiagnostic and disorder-specific iCBT,³⁵ adherence rates varied between 43% and 90%, indicating a discrepancy between treatment satisfaction and adherence. Research has shown that guided iCBT for anxiety disorders yielded higher acceptability in terms of adherence and

participant satisfaction.³⁴ However, the relevance of such features in outcomes of internet treatments appears indecisive. Insofar, clinicians should keep themselves up-to-date of recent developments in internet-delivered therapies for PD to decide on their suitability for patients.

Considering the broad scope of systematic reviews on several anxiety disorders,^{12-14,25,26,28,30,35,36} the rapidly growing evidence base and the heterogeneous assessment in studies, a narrative synthesis of the literature was performed to provide a rapid overview of current internet-delivered treatment for PD. This review aims at exploring the present evidence base on 1) the effectiveness of internet treatments for PD in comparison to a control condition as well as potential differences in outcomes between support formats or treatment approaches. Another purpose was to explore 2) indicators of acceptance of internet treatments, namely attrition and adherence rates as well as participant satisfaction.

METHODS

Eligibility criteria

This narrative review included papers targeting the effectiveness of internet treatments for PD, published in English peer-reviewed journals in the past five years. Based on the PICOS tool (Participants, Intervention, Comparator, Outcome, Study design),³⁹ the following inclusion criteria were defined:

- *Participants*: adults aged over 18 years, primary or secondary PD-diagnosis according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV or -V)
- *Intervention*: stand-alone, structured internet-delivered psychological treatment
- *Comparators*: (a) control condition (passive, active, CAU) or another active treatment arm with respect to (b) support format (unguided vs. guided) or (c) treatment approach (disorder-specific vs. transdiagnostic).
- *Outcomes*: (I) *primary outcomes*: reduction of panic symptom severity on a disorder-specific self-report measure at post-treatment, assessed via intention-to-treat (ITT)-analyses; (II) *secondary outcomes*: acceptability in terms of (a) attrition (randomized cases) and adherence rates (completion of all lessons/modules), as well as (b) participant satisfaction.
- *Study design*: only RCTs were included. Qualitative studies, re-examinations or secondary analyses of RCTs, study protocols and review articles were excluded.

Information sources, search and study selection

Electronic databases (PubMed/Medline, PSYINDEX) were systematically searched using the keywords (Medical Subject Headings; MeSH terms) “panic disorder” AND “internet” AND

“therapy” to identify RCTs of the past five years (2012/12/12–2017/12/10). To minimize the amount of irrelevant records in the PubMed search, “randomized controlled trial” and “last five years” were applied as filters. PSYINDEX was searched over the PubPsych platform using the filters “PSYINDEX,” “5 years,” “English,” and “journal article.” The last date searched was the 10th December 2017 for databases (PubMed, PSYINDEX) and the 29th December 2017 for additional sources [e.g., PubMedCentral (PMC), Cochrane Library, “Internet Interventions,” “Journal of Medical Internet Research,” reference lists of systematic reviews and meta-analyses] using further keywords such as “iCBT.” Risk of bias or study quality was not assessed. As a rule of thumb, high risk of bias was assumed in studies with an attrition rate of over 20%, whereas 5–20% represent a moderate risk of bias.⁴⁰

RESULTS

Study selection

The systematic database search resulted in 32 records, of which 22 stem from PubMed and 10 from PSYINDEX (Figure 1). After title screen, six of 22 records identified via PubMed

were excluded (i.e., study protocols,^{41–44} a Non-English paper,⁴⁵ and a study with children⁴⁶). Of the 10 records found through PSYINDEX, seven were duplicates and three not eligible (i.e., an off-topic conference,⁴⁷ a qualitative study,⁴⁸ and a review⁴⁹). Next, the abstracts of 16 records were screened. Eight records targeting no internet-delivered treatment,⁵⁰ blended treatment,³² PD not as the main target^{51–53} and secondary analyses^{54–56} were excluded. Then, after abstract reads of several papers found through hand search, four full texts were obtained that were found among related citations in PubMed,⁵⁷ PMC,^{19,58} reference lists and Cochrane Library.⁵⁹ After reading 12 full texts, four publications^{58–61} were excluded, because outcomes reported at post-treatment were not PD-specific. Finally, eight RCTs were included.

Study characteristics

The eight included papers were published between 2013 and 2017 (Table 1). Sample sizes ranged from n=63 to n=179. A total of 1,013 participants was recruited mostly from the general population in Australia,^{19,21} Germany,^{23,24,62} Switzerland,²⁴ Austria,²³ the Netherlands,⁶³ Sweden,⁶⁴ and Spain,⁵⁷ mainly online^{19,21,23,24,57,62–64} and traditional media advertise-

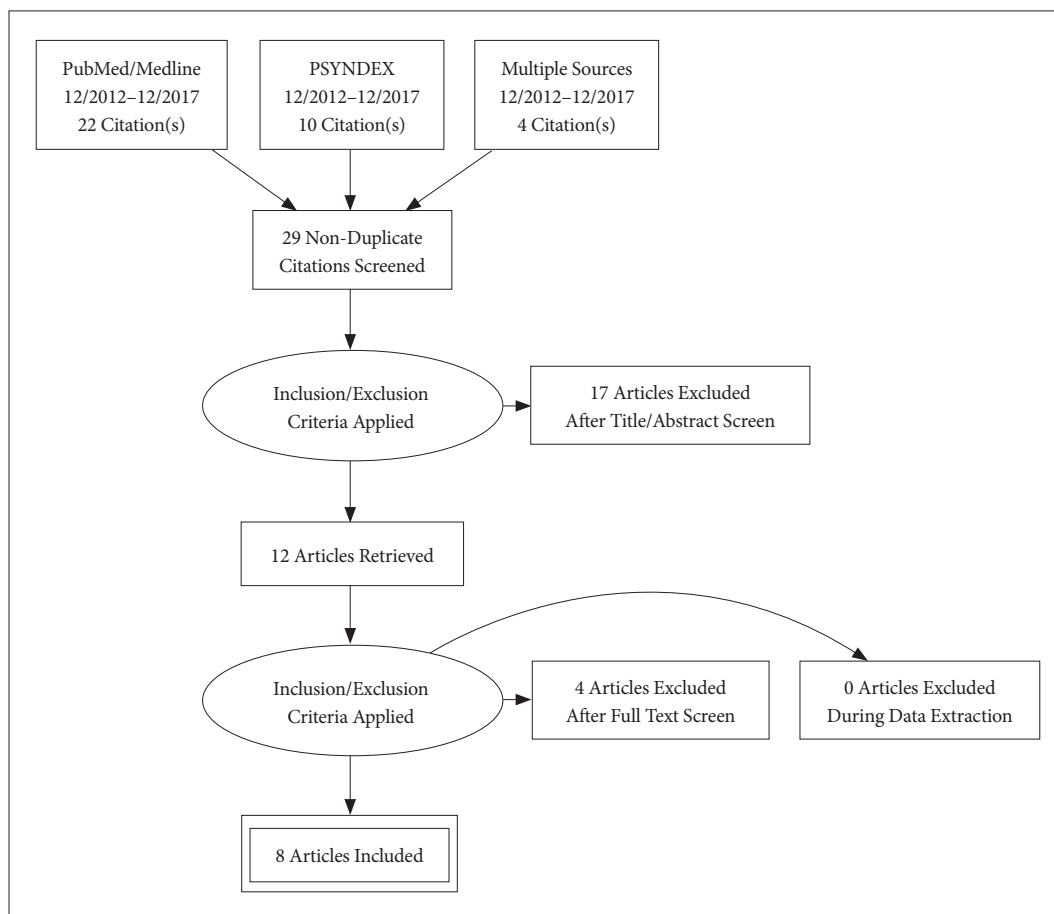


Figure 1. Flow chart diagram of study selection.

Table 1. Study characteristics

Study	Participants	Intervention	Comparators	Outcomes
Allen et al. ¹⁹	N=63 [†] Age over 18 years, with clinical PD (PDSS-SR ≥8), 100% with PD -Recruitment: online application -Setting: Internet, virtual clinic, Australia	Guided iCBT ("Panic Program") -Length: 8 weeks -Modules: 5 -Guidance: after lesson 1 and 2 (email or telephone) by clinician; time spent per iCBT-participant: M=4.23 min (SD=5.16)	RCT iCBT (N=27) vs. WLC (N=36) -IIT (PDSS-SR) -CC (2 satisfaction items)	Primary outcomes: -Effects at post-treatment (8 weeks)/ greater than WLC: yes -Effects maintained (3-months follow-up): yes Secondary outcomes: -Attrition: 29.75%; adherence: 63% -Satisfaction: (very) high
Berger et al. ²³	N=132 Age (M=35.1, SD=11.4, range 18-65 years), 56.1% female -Diagnosis of at least one anxiety disorder (33% PD/PDA) -14.4% under stable medication -Recruitment: newspaper advertisements and study website -Setting: Internet, Germany, Switzerland, Austria	Guided transdiagnostic iCBT for PD/PDA, SAD and GAD, and disorder-specific iCBT -Length: 8 weeks -Modules: 8 -Guidance: scheduled contact via email with Master students, a psychologist and a CBT-therapist; number of messages written by therapists: M=12.6 (SD=4.6)	RCT Transdiagnostic tailored treatment (TA, N=44) vs. disorder-specific standardized treatment (ST, N=44) vs. WLC (N=44) -IIT (ACQ, BSQ, MIA, MIB) -CC (CSQ-8)	Primary outcomes: -Effects at post-treatment (8 weeks)/ greater than WLC: yes* -Effects maintained (6-months follow-up): yes* Secondary outcomes: -Attrition: 9.8%; adherence: 70.5-75%* -Satisfaction: (very) high* *No difference between TA and ST
Berger et al. ²⁴	N=139 Age (M=42.0, SD=12.1, range 18-72 years), 70.5% female -Diagnosis of at least one anxiety disorder (64% PD/PDA, primary and secondary diagnoses) -41.0% currently in treatment; 33.8% taking medication -Recruitment: study website/self-selection (92.8%) and MDs -Setting: Internet, primary care, Germany, Switzerland	Unguided transdiagnostic tailored iCBT ("velibra") for PD/PDA, SAD and GAD -Length: 9 weeks -Modules: 6	RCT "CAU plus velibra" (N=70) vs. "CAU only" (face-to-face consultation with a MD) (N=69) -IIT (ACQ, BSQ, MIA, MIB) -CC (CSQ-8)	Primary outcomes: -Effects at post-treatment (9 weeks)/ greater than CAU: yes -Effects maintained (6-months follow-up): yes Secondary outcomes: -Attrition: 14%; adherence: 45.7% -Satisfaction: (very) high
Fogliati et al. ²¹	N=145 Age (M=41.40, SD=11.28, range 18-62 years), 79% female -Diagnosis of PD/PDA (91.0%), 40% currently taking medication -Recruitment: advertisements in major newspapers and NGOs -Setting: Internet, eCentreClinic, Australia	Disorder-specific iCBT ("Panic Course") and transdiagnostic iCBT ("Wellbeing Course"), self-guided and clinician-guided -Length: 8 weeks -Modules: 5 -Guidance: weekly contact via telephone or secured email by therapist; time spent per CG-participant: M=36.79 min (SD=21.35)	RCT Transdiagnostic (N=72) vs. disorder-specific iCBT (N=73), self-guided (N=73) vs. clinician-guided iCBT (N=72) -No control condition -IIT (PDSSR) -CC (2 satisfaction items)	Primary outcomes: -Effects at post-treatment (8 weeks)/ within-in effects: yes* -Effects maintained (3, 12, 24-months follow-up): yes* Secondary outcomes: -Attrition: 14-20%; adherence: 68-70%* -Satisfaction: (very) high* *No difference between conditions

Table 1. Study characteristics (continued)

Study	Participants	Intervention	Comparators	Outcomes
Ivanova et al. ⁶⁴	N=152 Age (M=35.29, SD=10.98), 64.5% female -Diagnosis of PD or SAD (25.7% primary PD, PDSS-SR ≥8), stable medication dosage for 3 months (42.8% previous or current medication), no ongoing psychological treatment -Recruitment: online and print media advertisement, Internet forums, notice-boards of health institutions -Setting: Internet, app, Sweden	Acceptance and Commitment Therapy (ACT), provided via the Internet and smartphone app ("ACT-smart"), self-guided and clinician-guided -Length: 8 weeks -Modules: 8 -Guidance: written feedback via app twice a week by Master students; time spent per CG-participant/week: about 15 min	RCT Guided (N=50) vs. unguided ACT (N=51) vs. WLC (N=51) -IIT (PDSSR) -Satisfaction: not assessed	Primary outcomes: -Effects at post-treatment (10 weeks)/greater than WLC: no* -Effects maintained (12-months follow-up): yes* Secondary outcomes: -Attrition: 15.8%; adherence: 7.8-40% (higher in the app in the guided group, not in the Internet platform) *No difference between formats
Oromendia et al. ⁵⁷	N=77 Age (M=40.7, SD=9.3, range 20-60 years), 68.8% female (100% PD) -Diagnosis PD/PDA primary for 1 year or more, stable medication: dosage/3 months -Recruitment: Google banners linked to searches about PD -Setting: Internet, Spain	Transdiagnostic iCBT ("Free from Anxiety") for PD, self-guided and clinician-guided -Length: 8 weeks -Modules: 8 -Guidance: weekly scheduled contact via telephone with psychologist; time spent per SPS-participant: M=69.43 min (SD=19.76)	RCT iCBT with non-scheduled psychological support (NPS, N=27) vs. scheduled psychological support (SPS, N=25) vs. WLC (N=25) -IIT (PDSS-SR) -CC (PDSS-SR) -Satisfaction: not assessed	Primary outcomes: -Effects at post-treatment (8 weeks)/greater than WLC: yes (both SPS and NPS; higher effects in SPS) -Effects maintained (6-months follow-up): yes (higher in SPS) Secondary outcomes: -Attrition: 14.3%; adherence: 44-68%
Schröder et al. ⁶²	N=179 Age (Intervention: M=36.6, SD=9.95, CAU: M=36.5, SD=10.26), 72% female -Diagnosis of at least one anxiety disorder (91.6% PD/ PDA, primary and secondary diagnoses), current psychotherapy (34.1%), on anxiolytics (41.4%). -Recruitment: moderated Internet forums for anxiety -Setting: Internet, Germany	Unguided transdiagnostic iCBT ("ConfID") for PD/PDA, agoraphobia, specific phobia and SAD -Length: 4 weeks -Modules: 4	RCT "CAU plus ConfID" (N=89) vs. "CAU only" (N=90) -IIT (PAS, APOI) -CC (PAS, APOI, adapted CSQ-8)	Primary outcomes: -Effects at post-treatment (4 weeks)/greater than CAU: yes (IIT, CC), attitude toward internet interventions moderated outcomes (IIT, CC); no follow-up Secondary outcomes: -Attrition: 28.5%; adherence: 52.8% (usage, at least once per week) -Satisfaction: moderate-high
Van Ballegooijen et al. ⁶³	N=126 Age (M=36.6, SD=11.4), 67.5% female -Subclinical-mild PD (PDSS-SR: 5-15), 78.2% with PD/PDA (primary and secondary diagnoses) -31.7% visited psychologist/psychiatrist, 34.1% on medication (past month) -Recruitment: health section of an online newspaper and Facebook -Setting: Internet, Netherlands	Guided disorder-specific iCBT ("Don't Panic Online") -Length: 8 weeks -Modules: 6 -Guidance: weekly mail by trained Master students; time spent per iCBT-participant: 1-2 hours	Pragmatic RCT iCBT (N=63) vs. WLC (N=63) -IIT (PDSS-SR) -CC (PDSS-SR) -Satisfaction: not assessed	Primary outcomes: -Effects at post-treatment/greater than WLC (12 weeks): no (IIT), yes (CC); no follow-up Secondary outcomes: -Attrition: 42.1%; adherence: 8%

†sample characteristics were not reported (paper with a scope on a second study with 330 patients). ACT: Acceptance and Commitment Therapy, APOI: Attitudes towards Psychological Online Interventions Questionnaire, ACQ: Agoraphobic Cognitions Questionnaire, BSQ: Body Sensations Questionnaire, CAU: care as usual, CC: Complete case analysis, CG: clinician-guided, CSQ-8: Client Satisfaction Questionnaire, iCBT: Internet-based Cognitive Behavioral Therapy, IIT: Intention-to-treat analysis, MIA/MIB: Mobility Inventory for Agoraphobia & Accompanied, MD: medical doctor, NPS: non-scheduled psychological support, PAS: Panic and Agoraphobia Scale, PD: panic disorder, PDA: panic disorder with agoraphobia, SPS: scheduled psychological support, ST: standardized treatment, TA: tailored treatment

ments^{21,23,64} via self-selection and in primary care.²⁴

Participants

Participants were aged between 18–72 years (mean age: 35–42). Most were female (range 56.1²³–79.0%²¹). Many had a University degree (range 31.3⁶²–57.0%²¹) and experience with psychological treatments (reported in four studies, 53²³–77.7%²⁴). The proportion of PD/PDA cases varied between 25.7%⁶⁴ and 100%.⁵⁷ Comorbidity was high in some studies (e.g. ^{62,63}).

Interventions

Out of web-based 10 interventions, four were disorder-specific^{19,21,23,63} and six transdiagnostic treatments [for a summary of contents, Supplementary Table 1 (in the online-only Data Supplement)].^{21,23,24,57,64,62} Nine interventions were based on CBT^{21,23,24,57,62,63} and one was ACT-based with CBT elements.⁶⁴ Most interventions had a length/availability of 8 weeks (range 4⁶²–12⁶³), with 4 to 8 lessons. Unguided self-help^{21,24,57,62,64} was provided with automated messages and support on demand. Guidance,^{19,21,23,57,63,64} via email or telephone varied in the average time spent from a few minutes¹⁹ up to one or two hours (per participant/program).^{21,57,63,64} Therapist qualifications differed (e.g., Master students, psychologists, CBT-therapists).

Comparators

Seven RCTs compared eight active treatments against a control condition, three studies guided vs. unguided formats, and two studies transdiagnostic vs. disorder-specific approaches (i.e., 13 comparisons) at post-treatment.

Outcomes

(I) The Panic Disorder Severity Scale Self-Report version (PDSS-SR) was used in five studies,^{19,21,57,63,64} multiple measures [Agoraphobic Cognitions Questionnaire (ACQ), Body Sensations Questionnaire (BSQ), Mobility Inventory for Agoraphobia & Accompanied (MIB, MIA)] in two studies^{23,24} and the Panic Agoraphobia Scale (PAS) in one study.⁶² (II) As shown in Table 1, all studies reported attrition (9.8–42.1%) and adherence rates (7.8–75%). Participant satisfaction was assessed in three studies^{23,24,62} using the Client Satisfaction Questionnaire (CQS-8) and in two studies^{19,63} using other measures.

Results of individual studies

Primary outcomes: effectiveness of internet treatments

Effectiveness of internet-delivered treatments vs. a control condition

Are disorder-specific internet treatments effective, when compared to a control condition?

Out of seven RCTs, three studies^{19,63} compared guided 8-week disorder-specific iCBT to WLC.

Allen et al.¹⁹ investigated the efficacy of the 8-week Australian iCBT “Panic Program” in 63 adults with at least moderate PD symptom severity. This 5-lesson short version of the 6-lesson program⁶⁵ involved brief telephone or email contacts with a therapist after the first two lessons. Results showed significant higher reductions in panic severity on the PDSS-SR of iCBT compared to WLC, with large between-group effect sizes (Hedge’s $g=0.97$). Self-report measures indicated more persons of the iCBT group (75%) fell into the non-clinical range with a PDSS-SR score less than 7 compared to WLC (29%).¹⁹

Berger et al.²³ evaluated the effects of guided 8-week iCBT transdiagnostic tailored and disorder-specific standardized iCBT (no names reported) compared to WLC in 132 German-speaking adults with at least one anxiety disorder (33.3% with PD/PDA). The disorder-specific intervention was significantly more effective than WLC, with medium-to-large effect sizes ranging from Cohen’s $d=0.54$ (MIA) to $d=0.97$ (ACQ), and significant clinical improvements of most participants with PD (62.5%).

In a pragmatic RCT, van Ballegooijen et al.⁶³ evaluated the 8-week Dutch iCBT “Don’t Panic Online” in 126 adults with sub-clinical or mild panic symptoms (78.2% with PD/PDA). In this 6-lesson iCBT program, trained Master-level students coached the iCBT group with weekly emails and support on demand. While IIT-analysis revealed no significant differences between the iCBT group and WLC on the PDSS-SR ($d=0.30$), significant higher reductions in the iCBT-group were conversely identified in CC-analyses, with medium between-group effect size ($d=0.73$), and large within-effect size ($d=1.23$).⁶³

Taken together, these disorder-specific iCBT appear being useful for motivated patients with clinically relevant PD symptoms.

Are transdiagnostic internet treatments effective, when compared to a control condition?

Out of five studies assessing transdiagnostic programs, two evaluated unguided and three studies guided internet treatments.

Berger et al.²⁴ investigated the effects of a 9-week transdiagnostic tailored unguided iCBT (“velibra”). They randomized 139 German-speaking adults (64.0% with PD/PDA, 45.3% primary diagnosis) either to “CAU plus velibra” or “CAU only,” whereas CAU involved a consultation with a physician in primary care. Program features contain daily automated messages, symptom tracking measures and personalization. As analyses of the PDA-subgroup showed, “velibra” was more effective than CAU only, with small between-group effect sizes ranging

between $d=0.22$ (MIB) and $d=0.45$ (ACQ). Significantly more participants assigned to “velibra” (38.3%) not met the diagnostic criteria for PD/PDA compared to participants receiving “CAU only” (9.8%).²⁴

Furthermore, Schröder et al.⁶² evaluated the effects of the unguided 4-week transdiagnostic German ConfID iCBT program (“CAU plus ConfID”) compared to a “CAU” (WLC) in 179 adults (91.6% with PD/PDA). Both participants assigned to ConfID or CAU/WLC were permitted to seek or maintain available therapies. Optional written feedback was provided by a psychologist and automated short message service (SMS). As expected, IIT-analyses demonstrated that this 4-module iCBT was more effective in reducing panic symptoms on the PAS than CAU, with medium effect size ($\eta_p^2=0.071$).⁶²

In the above outlined RCT by Berger et al.²³ the effects of guided 8-week iCBT transdiagnostic tailored iCBT were compared to WLC in 132 adults (29.5% with PD/PDA in the tailored condition). Guidance was provided as email-contact with five Master students, a trained psychologist and a CBT-therapist. Significant improvements in panic symptoms of the transdiagnostic approach were identified, with small to large between-group effect sizes ranging from $d=0.40$ (MIB) to $d=0.88$ (ACQ), as well as more persons with clinically relevant improvements (69.2%) compared to WLC (26.7%).²³

Oromendia et al.⁵⁷ evaluated the effects of the 8-week transdiagnostic iCBT “Free from Anxiety” as Spanish adaptation. They randomized 77 adults with PD either to iCBT with scheduled psychological support (clinician-guided), iCBT with non-scheduled psychological support (self-guided) or WLC. As assumed, iCBT was significantly more effective in reducing panic symptoms on the PDSS-SR in both the guided ($d=1.67$) and unguided format ($d=0.69$), when compared to WLC.⁵⁷

Finally, Ivanova et al.⁶⁴ investigated the effects of an 8-week transdiagnostic Swedish internet-delivered ACT with a supplemented smartphone app (“ACT-smart”) in 152 adults (25.7% suffering primarily from PD). This 8-module internet-delivered ACT was, however, ineffective compared to WLC in reducing panic symptoms ($d=0.05$), but was effective in SAD and general anxiety. Nevertheless, the within-group effect sizes were large for the treated group ($d=1.00$) on the PDSS-SR, and 25.9% of participants with PD clinically improved.⁶⁴

Hence, the outlined five studies suggested that both guided and unguided transdiagnostic iCBT programs are effective.

To summarize, five out of seven RCTs (8 comparisons) confirmed the effectiveness of iCBT programs differing in conditions (e.g., support format, treatment approach, and duration). Moreover, all five studies assessing follow-up indicated the maintenance of treatment gains with large within-in effect sizes at 3-month,¹⁹ 6 month^{23,24,57} and 12 months.⁶⁴

Effectiveness of therapist-guided vs. unguided internet-delivered treatments

Are guided treatments superior to unguided treatments?

Three RCTs directly compared support formats.

In the aforementioned study on “Free from Anxiety” by Oromendia et al.,⁵⁷ participants of the clinician-guided -group were contacted weekly via telephone by a psychologist (total time spent per participant, $M=69.43$ min, $SD=19.76$). Participants in the self-guided -group received weekly mails and support on demand. Analyses revealed significantly higher reductions of panic severity on the PDSS-SR in the guided group ($n=25$) compared to the unguided group ($n=25$), with a large between-group effect size ($d=1.18$), and a significantly higher number of participants with clinically important improvements in panic symptoms (70.8% in the guided group vs. 20.8% in the unguided group). Within effects were large (guided with $d=1.30$; unguided with $d=2.40$) and retained in both groups at the 6-month follow-up.⁵⁷

In contrast, two studies^{21,64} found no relevant impact of support format.

Fogliati et al.²¹ assessed 8-week clinician-guided and self-guided iCBT (“Panic Course” and “Wellbeing Course”) in 145 adults from Australia (91% with PD). Guidance was provided as weekly clinician-contact via telephone or secure email (total time spent per participant: $M=36.79$ minutes, $SD=21.35$). Participants in the self-guided iCBT were monitored and received weekly automated emails as well as support on demand. No significant differences between support formats on the PDSS-SR were identified; large within-in effects were found among persons with PD assigned to clinician-guided ($n=65$, $d=0.71$) and self-guided iCBT ($n=67$, $d=1.09$). Improvements were maintained with large within-in effect sizes over the course of 24 months.²¹

In the above mentioned study on internet-delivered “ACT-smart” by Ivanova et al.,⁶⁴ guidance was provided twice per week by seven trained and weekly supervised Master students as written feedback via the app (time spent: about 15 minutes per participant and week) in addition to automated messages. This study found no significant difference between participants with primary PD ($n=20$ at post-treatment) in the guided group ($n=9$, $d=1.18$) and unguided group ($n=11$, $d=0.99$) on the PDSS-SR. Effects were maintained at 12-month follow-up.⁶⁴

Overall, the results indicate that both delivery modes are comparable in outcomes.

Effectiveness of transdiagnostic vs. disorder-specific internet-delivered treatments

Are transdiagnostic treatments superior to disorder-specific treatments?

Two previously described RCTs^{21,23} investigated differences between both treatment approaches.

Berger et al.²³ compared the effects of transdiagnostic tailored (n=44) with disorder-specific standardized iCBT (n=44). In the disorder-specific condition, 27.7% received access to PD/PDA-specific contents. Results showed no significant differences in PD-specific measures. Within-in effect sizes were large (transdiagnostic with $d=1.09$ and disorder-specific with $d=1.12$). However, the sample mainly consisted of patients with Social Anxiety Disorder (SAD; 86%).²³

Fogliati et al.²¹ assessed differences between the 5-session disorder-specific “Panic Course” (n=68 with PD) and the transdiagnostic “Wellbeing Course” (n=64 with PD). They found no significant differences between the approaches on the PDSS-SR; both groups improved significantly from baseline to post-treatment (disorder-specific, $d=0.79$; transdiagnostic, $d=0.97$).²¹

Insofar, both studies did not indicate better outcomes of transdiagnostic approaches.

Secondary outcomes: acceptability of internet treatments

Attrition and adherence

As shown in Table 1, the attrition rates and adherence varied largely, with the lowest attrition rate was found in a guided ICBT (with 9.8%).²³ In contrast, three studies reported an attrition rate of more than 28% (i.e., ConfID, Panic Program, Don't Panic Online). For instance, a high attrition rate (28.5%) was found in the study on the 4-week unguided “ConfID,”⁶² in which only 52.8% indicated to interact more than once a week with “ConfID”-the most frequently stated reason for non-adherence was lack of time (47.4%). In the RCT on the guided “Panic Program” (29.75%),¹⁹ adherence amounted to 63%. Finally, the highest attrition rate (42.1%) was reported in the study on the guided 8-week “Don't Panic Online,”⁶³ in which only 8% of the participants finished all 6 lessons. Most frequently reported reasons for dropping out included time constraints, life events and symptom severity.⁶³ Remarkably, in the unguided “velibra” program,²⁴ the attrition rate was much lower (14%), but the adherence rate amounting to 45.7% was poorer than in other studies with more dropouts.

Are guided internet treatments superior to unguided treatments in improving adherence?

The study on “Free from Anxiety”⁵⁷ showed a moderate attrition rate (14.3%), whereas, of the 20.8% dropping out of treatment, a significant lower rate was found in the clinician-guided

group (8.3%) compared to the self-guided group (33.3%). Adherence was accordingly significantly higher in the clinician-guided-group, with 68% completing the entire program (vs. 44% of the self-guided group).⁵⁷

Moreover, a positive effect of guidance was also found in another RCT: In the study on internet-delivered ACT by Ivanova et al.⁶⁴ (with an attrition rate of 15.8%), significantly more participants in the guided group completed all 8 modules (30%) compared to the unguided group (7.8%) in the app; conversely, the difference in adherence in the internet platform between guided group (40%) and the unguided group (29.4%) was not significant. Moreover, significant more entrances per week in the app were found in the guided group.⁶⁴

In the RCT by Fogliati et al.,²¹ the attrition rates ranged from 14% in the self-guided and 18% in the clinician-guided iCBT condition; adherence rates in terms of completion of all 5 lessons did not significantly differ between the self-guided (68%) and the clinician-guided (69%) condition.

Overall, two out of three studies showed benefits of guidance at least for adherence.

Are transdiagnostic internet treatments superior to disorder-specific treatments in improving adherence?

In the study on guided iCBT by Berger et al.²³ (attrition rate of 9.8%), adherence amounted to 75% in the transdiagnostic condition and 70.5% in the disorder-specific condition, with no significant difference in the average number of completed sessions (7 out of 8).²³

In the RCT by Fogliati et al.,²¹ the attrition rates ranged from 11% (disorder-specific “Panic Course”) to 20% (transdiagnostic “Wellbeing Course”); the adherence rate in terms of completion of all 5 lessons between 68% (transdiagnostic) and 70% (disorder-specific) was also comparable across conditions.

Participant satisfaction

Treatment satisfaction was assessed in five RCTs, all with positive findings. Accordingly, three RCTs from German-speaking countries using the CSQ-8^{23,24,62} indicated an overall relatively high participant satisfaction, in the unguided “velibra” (at the 6-month follow-up²⁴) and in both guided tailored transdiagnostic and standardized disorder-specific iCBT, with no significant difference between both approaches.²³ Furthermore, Schröder et al.⁶² used an adapted CSQ-8 that indicated that most participants were satisfied with the quality of “ConfID” (73.6%).

Different acceptability measures were used in both Austrian studies.^{19,21} In the study by Allen et al.,¹⁹ 93% of the participants indicated being mostly or very satisfied with the “Panic Program,” and 87% reported being mostly or very confident

to recommend the course to a friend with a similar problem.

Additionally, Fogliati et al.²¹ identified no significant differences in satisfaction ratings between support formats and approaches (“Wellbeing Course” and “Panic Course”); most (96–100%) reported they would recommend the course to others and that it was worth their time (93–95%).

Overall, there was a consistently high satisfaction across treatment modalities, whereas attrition and adherence rates differed.

DISCUSSION

Summary of evidence and implications

This review aimed at exploring the efficacy and acceptability of different internet-delivered treatment options for panic symptoms. Key findings and implications will be discussed next.

Effectiveness of internet-delivered treatments

Taken together, five out of seven RCTs showed significant improvements in panic symptoms in guided disorder-specific iCBT^{19,23} and in both unguided and guided transdiagnostic iCBT interventions,^{19,23,24,57,62,66} when compared to a control condition. These findings contribute to prior research targeting iCBT for anxiety disorders.^{14,30,38} Future studies should thus focus on determining specific therapeutic effects of iCBT, for instance, by using study designs combining active and passive control conditions.^{19,24} Another option could be to compare the efficacy of specific contents or modules such of internet treatments such as exposure or relaxation exercises in iCBT. Moreover, the evidence base on predictors of outcome in iCBT for PD is limited.⁶⁷ Interestingly, the study on “ConfID”⁶² showed that a more positive attitude at baseline moderated therapeutic outcomes. A further investigation of the impact of pre-treatment attitudes in the response to iCBT could be therefore useful to decide, which patient might most likely benefit.⁶⁸ Another interesting finding was that a good therapeutic working alliance could be established in different internet treatment approaches,²³ which is consistent other research.^{66,69} Overall, findings suggest the helpfulness of internet treatments for PD patients with a preference for online self-help as stand-alone treatments and for those wishing to bridge waiting times for face-to-face therapy.

In contrast, IIT-analyses indicated no significant improvements in panic symptoms in two included RCTs.^{63,64} One of these studies assessed “Don’t Panic Online”⁶³ in a sample with mild or subclinical PD cases and proved to be effective in reducing panic symptoms only among program completers. In this context, van Ballegooijen et al.⁶³ noted the high proportion of comorbidity with Major Depressive Disorder (42.7%)

might have contributed to poor -adherence rates. Furthermore, Allen et al.¹⁹ argued that disorder-specific iCBT might be less helpful in subclinical PD. The other RCT⁶⁴ with no meaningful effects for PD evaluated “ACT-smart” with a supplemented app. Ivanova et al.⁶⁴ assumed the small proportion of PD cases in their study, the novelty of ACT protocols translated to internet-delivery and a probable superiority of iCBT over internet-delivered ACT for PD as possible reasons for non-significant findings.⁶⁴ Indeed, the few published studies on internet-delivered ACT mostly targeted depression.¹⁷ Considering the scarce evidence base on the effectiveness of internet-delivered third-wave CBT programs on the one hand and the popularity of such trainings on the other hand, further research is recommended.¹⁵ Moreover, given the lack of evidence-based apps for PD,⁷⁰ a further investigation of “ACT-smart” appears worthwhile. In addition, other third-wave CBT components such as mindfulness exercises have been successfully applied in several internet treatments like “velibra” or “Free from Anxiety.”

Regarding support formats, only one RCT⁵⁷ of three found significant improvements in panic symptoms and adherence rates in favor of guided treatments. This is in accordance with earlier research.^{22,71} Oromendia et al.⁵⁷ assumed a positive impact of the scheduled support on participants’ commitment to “Free from Anxiety,” which might have increased adherence to treatment and therapeutic outcomes. Different reasons appear reasonable for the other two studies^{21,64} that found no significant difference between support formats in outcomes. Fogliati et al.²¹ argued that “new generation” iCBT work well as self-guided format, since they are grounded on well-established protocols, evaluated over several clinical trials and typically involve measures that aim at monitoring and engaging patients, such as automated messages.²¹ Another possibility is the selection bias. For instance, in the study on the unguided “velibra,”²⁴ Berger et al.²⁴ argued that the need for consulting a primary care physician might have increased the threshold for less motivated patients. This assumption of selection bias is also supported by the fact that in some studies^{21,57,62} only few participants in self-guided conditions accepted the offer of clinician-guidance on demand. Furthermore, although there were differences in the support quantity and modality in guided interventions, no patterns with outcomes or adherence appeared evident. Of the studies with a comparable average time spent per participant, some were effective,⁵⁷ whereas others⁶³ were not. In fact, the current state of research is incoherent, especially regarding the dose-dependency of support in treatment outcomes.²² A systematic review²² found that guidance appears to be a helpful feature in internet treatments, but the impact they identified was smaller than stated earlier. Yet, studies on underlying process-

es and specific components making different support formats effective and acceptable are scarce.²¹ For instance, in contrast to face-to-face treatments research indicates that the qualification of online-therapists appears to be irrelevant for outcomes.^{22,72} For decisions on suitable treatment options for PD, patients' preferences should be considered.²⁰ For instance, given a preference of many adults for self-help to manage milder psychological problems on one's own as a barrier to seek help face-to-face,⁷³ unguided programs can be recommended for subclinical symptoms and prevention.²² It could be thus interesting to explore which subpopulations prefer guidance to provide stepped care models for PD.³² Surveys further suggest that many persons prefer therapist-guided IPT and face-to-face services in case of more severe emotional problems.⁷⁴ Treatment preferences of patients with different symptomatology should be investigated to provide more or better suitable therapy options for specific subpopulations in routine care.

Furthermore, although of the most reviewed interventions were based on a transdiagnostic approach, only two studies^{21,23} compared outcomes directly with the more established disorder-specific approach. Both studies showed no significant difference between the approaches. This is in contrast to findings of a review²¹ that indicated a superiority of disorder-specific over transdiagnostic iCBT for anxiety disorders. It would be therefore interesting to explore the role of perceived benefits across treatment approaches from the perspective of patients.³⁵ Because tailoring allows for accurate assignment to treatment with respect to comorbid anxiety disorders, tailored transdiagnostic treatments have advantages for the dissemination of iCBT in routine care.²⁴ Transdiagnostic treatments can work well as self-guided format,^{24,62} which is a clear benefit for the dissemination regarding treatment gaps.²¹ Thus, this combination appears efficient to provide additional treatment options.

Acceptability of internet-delivered treatments

Attrition rates varied largely across the RCTS. Interestingly, both the lowest (9.8%)²³ and the highest (42.1%)⁶³ dropout rate were found in different therapist-guided 8-week iCBT programs.

Relatively high attrition rates are commonly reported in iCBT trials for anxiety disorders.²⁶ For instance, in reviews on internet-based treatments for different diagnoses dropout rates were between 2% and 89%, with a weighted mean of 31% (19 studies),⁷⁵ between 1% and 50% (23 studies),⁷⁶ or between 0% and 55% (13 studies).²⁹ In addition, adverse events as potential reasons for dropouts were not directly reported, which is a common issue in iCBT research.^{14,77}

The present review also found variance in adherence rates, ranging from 7.8% to 75%. For instance, in the study on the

5-lesson "Panic Program," 19 adherence (63%) was lower than in a previous trial using a 6-lesson version (79%).⁶⁵ This is interesting, because the briefer version aimed at improving adherence; the same study reported that the 5-lesson "Panic Program" was also effective ($g=0.55$), when delivered in a primary care setting ($n=330$ patients), albeit the adherence rate was lower (56.1%) than in the included RCT.¹⁹ Clearing the relevance of iCBT length need further investigation. Consistent with other studies,⁶⁰ two included studies^{62,63} identified lack of time as a barrier to complete iCBT programs. Ivanova et al.⁶⁴ supposed that the relatively low degree of full adherence in the "ACT-smart" study could be attributed to multiple log-ins at different platforms and devices. Usability issues related to delivery modes (e.g., internet-based, computerized or smartphone-delivered) as reasons for non-adherence need detailed exploration. Moreover, minimal guidance may have improved adherence in two studies,^{64,57} and clinical effects in PD in one study.⁵⁷ According to Mewton et al.,¹² guidance in iCBT is not needed for immediate improvements, but could be essential for the maintenance of clinical effects and adherence. In routine care, a combination of online and face-to-face format (i.e., blended treatments) can be useful as they can improve adherence or lower dropout rates.⁷⁸

In accordance with prior research,³⁸ five RCTs that assessed participant satisfaction endorsed a relatively high acceptance of internet treatment with different modalities. Earlier research¹⁴ indicated a high participant satisfaction in therapist-guided iCBT for anxiety disorders. However, in one included study,²¹ no difference in satisfaction was found between support formats. Furthermore, ratings stem from CC-analyses and might be thus biased towards higher satisfaction. Future studies should evaluate the (dis-) satisfaction of non-completers to improve the acceptability of Internet treatments. This could help identifying reasons for the discrepancy between high satisfaction and suboptimal adherence.

Limitations

This review has several limitations. On the study level, self-selection of participants limits the external validity. Samples mainly consisted of women who are at a higher risk for PD.² Three studies with transdiagnostic scope had a low percentage of PD/PDA cases in relation to SAD cases, although this reflects epidemiological distribution.^{23,24,64} Different confounding factors were not strictly controlled: although studies excluded severe mental illness, most made no restrictions made regarding ongoing pharmacotherapy (except for a stable dosage) or psychotherapy. Another issue is the limited availability of evidence-based programs. Furthermore, all studies used self-report measures. The absence of a control condition in the study by Fogliati et al.²¹ was another limitation. Attrition

bias was another drawback in some studies. Nonetheless, the study quality was overall high. On the review basis, it should be noted that this was not a systematic review (c.f.⁷⁹). Risk of bias is, for instance, increased due to the omission of a second reviewer. Additionally, the narrowed search strategy (e.g., time span) resulted in a selection of fewer studies. However, several studies on iCBT for PD published before December 2012 (e.g.^{65,80-84}) were already analyzed in previous reviews.¹⁴ Another limitation is the restriction to few MeSH terms considering the inconsistent terminology in the literature.⁷⁴ Thus, “internet treatment” was used as umbrella term for several delivery modes. Additionally, no MeSH terms for secondary outcomes were systematically searched. Also, only studies with mainly Caucasian samples were identified, albeit, to the author’s knowledge, few iCBT publications have investigated cross-cultural⁸⁵ or Asian samples.⁸⁶ Moreover, seven out of 10 interventions were Non-English. Finally, consistent with earlier reviews,^{14,26,35} heterogeneity regarding the measurement hampered comparisons between studies.

Conclusions

Overall, this article illustrated different effective and well-accepted evidence-based internet-delivered psychological treatments for panic disorder. Considering challenges related to treating comorbid anxiety disorders in times of treatment gaps, self-guided transdiagnostic iCBT programs appear to be efficient options for the large-scale dissemination in primary care. However, the discrepancy between high acceptability and slow uptake as well as the unclear role of patients’ preferences require further investigation. Hence, clinicians should be informed about the latest advances in order to guide patients regarding the usefulness of internet-delivered treatments.

Supplementary Materials

The online-only Data Supplement is available with this article at <https://doi.org/10.30773/pi.2018.06.26>.

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